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(54) Title: METHODS FOR IDENTIFYING RISK OF BREAST CANCER AND TREATMENTS THEREOF

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(57) Abstract: Provided herein are methods for identifying risk of breast cancer in a subject and/or a subject at risk of breast cancer, reagents and kits for carrying out the methods, methods for identifying candidate therapeutics for treating breast cancer, and therapeutic methods for treating breast cancer in a subject. These embodiments are based upon an analysis of polymorphic variations in nucleotide sequences within the human genome.

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METHODS FOR IDENTIFYING RISK OF BREAST CANCER AND TREATMENTS THEREOF

Field of the Invention

[0001] The invention relates to genetic methods for identifying risk of breast cancer and treatments that specifically target the disease.

Background

[0002] Breast cancer is the third most common cancer, and the most common cancer in women, as well as a cause of disability, psychological trauma, and economic loss. Breast cancer is the second most common cause of cancer death in women in the United States, in particular for women between the ages of 15 and 54, and the leading cause of cancer-related death (Forbes, *Seminars in Oncology*, vol.24(1), Suppl 1, 1997: pp.S1-20-S1-35). Indirect effects of the disease also contribute to the mortality from breast cancer including consequences of advanced disease, such as metastases to the bone or brain. Complications arising from bone marrow suppression, radiation fibrosis and neutropenic sepsis, collateral effects from therapeutic interventions, such as surgery, radiation, chemotherapy, or bone marrow transplantation-also contribute to the morbidity and mortality from this disease.

[0003] While the pathogenesis of breast cancer is unclear, transformation of normal breast epithelium to a malignant phenotype may be the result of genetic factors, especially in women under thirty (Miki, *et al.*, *Science*, 266: 66-71 (1994)). However, it is likely that other, non-genetic factors also have a significant effect on the etiology of the disease. Regardless of its origin, breast cancer morbidity increases significantly if it is not detected early in its progression. Thus, considerable efforts have focused on the elucidation of early cellular events surrounding transformation in breast tissue. Such efforts have led to the identification of several potential breast cancer markers. For example, alleles of the *BRCA1* and *BRCA2* genes have been linked to hereditary and early-onset breast cancer (Wooster, *et al.*, *Science*, 265: 2088-2090 (1994)). However, *BRCA1* is limited as a cancer marker because *BRCA1* mutations fail to account for the majority of breast cancers (Ford, *et al.*, *British J. Cancer*, 72: 805-812 (1995)). Similarly, the *BRCA2* gene, which has been linked to forms of hereditary breast cancer, accounts for only a small portion of total breast cancer cases.

Summary

[0004] It has been discovered that certain polymorphic variations in human genomic DNA are associated with the occurrence of breast cancer. In particular, polymorphic variants in loci containing

DLG1, *KIAA0783*, *DPF3* and *CENPC1* regions in human genomic DNA have been associated with risk of breast cancer.

[0005] Thus, featured herein are methods for identifying a subject at risk of breast cancer and/or a risk of breast cancer in a subject, which comprises detecting the presence or absence of one or more polymorphic variations associated with breast cancer in genomic regions described herein in a human nucleic acid sample. In an embodiment, two or more polymorphic variations are detected in two or more regions selected from the group consisting of *DLG1*, *KIAA0783*, *DPF3* and *CENPC1*. In certain embodiments, 3 or fewer, or 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 or fewer polymorphic variants are detected.

[0006] Also featured are nucleic acids that include one or more polymorphic variations associated with the occurrence of breast cancer, as well as polypeptides encoded by these nucleic acids. Further, provided is a method for identifying a subject at risk of breast cancer and then prescribing to the subject a breast cancer detection procedure, prevention procedure and/or a treatment procedure. In addition, provided are methods for identifying candidate therapeutic molecules for treating breast cancer and related disorders, as well as methods for treating breast cancer in a subject by diagnosing breast cancer in the subject and treating the subject with a suitable treatment, such as administering a therapeutic molecule.

[0007] Also provided are compositions comprising a breast cancer cell and/or *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acid with a RNAi, siRNA, antisense DNA or RNA, or ribozyme nucleic acid designed from a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleotide sequence. In an embodiment, the nucleic acid is designed from a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleotide sequence that includes one or more breast cancer associated polymorphic variations, and in some instances, specifically interacts with such a nucleotide sequence. Further, provided are arrays of nucleic acids bound to a solid surface, in which one or more nucleic acid molecules of the array have a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleotide sequence, or a fragment or substantially identical nucleic acid thereof, or a complementary nucleic acid of the foregoing. Featured also are compositions comprising a breast cancer cell and/or a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide, with an antibody that specifically binds to the polypeptide. In an embodiment, the antibody specifically binds to an epitope in the polypeptide that includes a non-synonymous amino acid modification associated with breast cancer (e.g., results in an amino acid substitution in the encoded polypeptide associated with breast cancer). In certain embodiments, the antibody specifically binds to an epitope that comprises a glutamine at amino acid position 278 in SEQ ID NO: 9 of a *DLG1* polypeptide or a glycine at amino acid position 389 in SEQ ID NO: 12 of a *CENPC1* polypeptide.

Brief Description of the Figures

[0008] Figures 1A-1T show a genomic nucleotide sequence for an *DLG1* region. The genomic nucleotide sequence is set forth in SEQ ID NO: 1. The following nucleotide representations are used

throughout: “A” or “a” is adenosine, adenine, or adenylic acid; “C” or “c” is cytidine, cytosine, or cytidylic acid; “G” or “g” is guanosine, guanine, or guanylic acid; “T” or “t” is thymidine, thymine, or thymidylic acid; and “I” or “i” is inosine, hypoxanthine, or inosinic acid. Exons are indicated in italicized lower case type, introns are depicted in normal text lower case type, and polymorphic sites are depicted in bold upper case type. SNPs are designated by the following convention: “R” represents A or G, “M” represents A or C; “W” represents A or T; “Y” represents C or T; “S” represents C or G; “K” represents G or T; “V” represents A, C or G; “H” represents A, C, or T; “D” represents A, G, or T; “B” represents C, G, or T; and “N” represents A, G, C, or T.

[0009] Figures 2A-2Z show a genomic nucleotide sequence of a *KIAA0783* region. The genomic nucleotide sequence is set forth in SEQ ID NO: 2.

[0010] Figures 3A-3X show a genomic nucleotide sequence of a *DPF3* region. The genomic nucleotide sequence is set forth in SEQ ID NO: 3.

[0011] Figures 4A-4Y show a genomic nucleotide sequence of a *CENPC1* region. The genomic nucleotide sequence is set forth in SEQ ID NO: 4.

[0012] Figure 5 shows a coding nucleotide sequence (cDNA) for *DLG1*. The nucleotide sequence is set forth in SEQ ID NO: 5.

[0013] Figure 6 shows a coding nucleotide sequence (cDNA) for *KIAA0783*. The nucleotide sequence is set forth in SEQ ID NO: 6.

[0014] Figure 7 shows a coding nucleotide sequence (cDNA) for *DPF3*. The nucleotide sequence is set forth in SEQ ID NO: 7.

[0015] Figure 8 shows a coding nucleotide sequence (cDNA) for *CENPC1*. The nucleotide sequence is set forth in SEQ ID NO: 8.

[0016] Figure 9 shows an amino acid sequence for a *DLG1* polypeptide, which is set forth in SEQ ID NO: 9.

[0017] Figure 10 shows an amino acid sequence for a *KIAA0783* polypeptide, which is set forth in SEQ ID NO: 10.

[0018] Figure 11 shows an amino acid sequence for a *DPF3* polypeptide, which is set forth in SEQ ID NO: 11.

[0019] Figure 12 shows an amino acid sequence for a *CENPC1* polypeptide, which is set forth in SEQ ID NO: 12.

[0020] Figures 13-16 show proximal SNPs in *DLG1*, *KIAA0783*, *DPF3* and *CENPC1* loci in genomic DNA. The position of each SNP on the chromosome is shown on the x-axis and the y-axis provides the negative logarithm of the p-value comparing the estimated allele to that of the control group. Also shown in the figure are exons and introns of the genes in the approximate chromosomal positions. The figure indicates that polymorphic variants associated with breast cancer are in linkage disequilibrium in the following regions: the region spanning positions 7938-59808 in SEQ ID NO: 1;

the region spanning positions 10511-98107 in SEQ ID NO: 2; the region spanning positions 160-72752 in SEQ ID NO: 3; and the region spanning positions 196-74909 in SEQ ID NO: 4.

Detailed Description

[0021] It has been discovered that polymorphic variations in the *DLG1*, *KIAA0783*, *DPF3* and *CENPC1* regions described herein are associated with an increased risk of breast cancer.

[0022] The gene *DLG1* (discs, large homolog 1 (Drosophila)) is also referenced as synapse-associated protein 97, hdlg, SAP97. *DLG1* has been mapped to chromosomal position 3-q29. In Drosophila more than 50 genes have been identified that lead to loss of cell proliferation control, indicating that they are tumor suppressor genes. Many of these genes have been cloned and sequenced, and most have clear mammalian homologs. The Drosophila 'discs large' tumor suppressor protein, Dlg, is the prototype of a family of proteins termed MAGUKs (membrane-associated guanylate kinase homologs). MAGUKs are localized at the membrane-cytoskeleton interface, usually at cell-cell junctions, where they appear to have both structural and signaling roles. They contain several distinct domains, including a modified guanylate kinase domain, an SH3 motif, and 1 or 3 copies of the DHR (GLGF/PDZ) domain. Recessive lethal mutations in the 'discs large' tumor suppressor gene interfere with the formation of septate junctions (thought to be the arthropod equivalent of tight junctions) between epithelial cells, and they also cause neoplastic overgrowth of imaginal discs, suggesting a role for cell junctions in proliferation control.

[0023] The gene *KIAA0783* also is known as PHF14 and PHD finger protein 14. *KIAA0783* has been mapped to chromosomal position 7p21.3. The protein encoded by this gene is a novel gene with unknown function. Being a zinc finger protein, it likely a transcription factor.

[0024] The gene *DPF3* (D4, zinc and double PHD fingers, family 3) also is known as CERD4, cer-d4, FLJ14079, and 2810403B03Rik. *DPF3* is a Rho family guanine-nucleotide exchange factor. *DPF3* has been mapped to chromosomal position 14q24.3-q31.1.

[0025] The gene *CENPC1* (centromere protein C1) also is known as Centromere autoantigen C1. *CENPC1* has been mapped to chromosomal position 4q12-q13.3. *CENPC1* is a centromere autoantigen and a component of the inner kinetochore plate. The protein is required for maintaining proper kinetochore size and a timely transition to anaphase. A putative pseudogene exists on chromosome 12.

Breast Cancer and Sample Selection

[0026] Breast cancer is typically described as the uncontrolled growth of malignant breast tissue. Breast cancers arise most commonly in the lining of the milk ducts of the breast (ductal carcinoma), or in the lobules where breast milk is produced (lobular carcinoma). Other forms of breast cancer include Inflammatory Breast Cancer and Recurrent Breast Cancer. Inflammatory breast cancer is a

rare, but very serious, aggressive type of breast cancer. The breast may look red and feel warm with ridges, welts, or hives on the breast; or the skin may look wrinkled. It is sometimes misdiagnosed as a simple infection. Recurrent disease means that the cancer has come back after it has been treated. It may come back in the breast, in the soft tissues of the chest (the chest wall), or in another part of the body.

[0027] As used herein, the term “breast cancer” refers to a condition characterized by anomalous rapid proliferation of abnormal cells in one or both breasts of a subject. The abnormal cells often are referred to as “neoplastic cells,” which are transformed cells that can form a solid tumor. The term “tumor” refers to an abnormal mass or population of cells (*i.e.* two or more cells) that result from excessive or abnormal cell division, whether malignant or benign, and pre-cancerous and cancerous cells. Malignant tumors are distinguished from benign growths or tumors in that, in addition to uncontrolled cellular proliferation, they can invade surrounding tissues and can metastasize. In breast cancer, neoplastic cells may be identified in one or both breasts only and not in another tissue or organ, in one or both breasts and one or more adjacent tissues or organs (*e.g.* lymph node), or in a breast and one or more non-adjacent tissues or organs to which the breast cancer cells have metastasized.

[0028] The term “invasion” as used herein refers to the spread of cancerous cells to adjacent surrounding tissues. The term “invasion” often is used synonymously with the term “metastasis,” which as used herein refers to a process in which cancer cells travel from one organ or tissue to another non-adjacent organ or tissue. Cancer cells in the breast(s) can spread to tissues and organs of a subject, and conversely, cancer cells from other organs or tissue can invade or metastasize to a breast. Cancerous cells from the breast(s) may invade or metastasize to any other organ or tissue of the body. Breast cancer cells often invade lymph node cells and/or metastasize to the liver, brain and/or bone and spread cancer in these tissues and organs. Breast cancers can spread to other organs and tissues and cause lung cancer, prostate cancer, colon cancer, ovarian cancer, cervical cancer, gastrointestinal cancer, pancreatic cancer, glioblastoma, bladder cancer, hepatoma, colorectal cancer, uterine cervical cancer, endometrial carcinoma, salivary gland carcinoma, kidney cancer, vulval cancer, thyroid cancer, hepatic carcinoma, skin cancer, melanoma, ovarian cancer, neuroblastoma, myeloma, various types of head and neck cancer, acute lymphoblastic leukemia, acute myeloid leukemia, Ewing sarcoma and peripheral neuroepithelioma, and other carcinomas, lymphomas, blastomas, sarcomas, and leukemias.

[0029] Breast cancers arise most commonly in the lining of the milk ducts of the breast (ductal carcinoma), or in the lobules where breast milk is produced (lobular carcinoma). Other forms of breast cancer include Inflammatory Breast Cancer and Recurrent Breast Cancer. Inflammatory Breast Cancer is a rare, but very serious, aggressive type of breast cancer. The breast may look red and feel warm with ridges, welts, or hives on the breast; or the skin may look wrinkled. It is sometimes misdiagnosed as a simple infection. Recurrent disease means that the cancer has come back after it

has been treated. It may come back in the breast, in the soft tissues of the chest (the chest wall), or in another part of the body. As used herein, the term “breast cancer” may include both Inflammatory Breast Cancer and Recurrent Breast Cancer.

[0030] In an effort to detect breast cancer as early as possible, regular physical exams and screening mammograms often are prescribed and conducted. A diagnostic mammogram often is performed to evaluate a breast complaint or abnormality detected by physical exam or routine screening mammography. If an abnormality seen with diagnostic mammography is suspicious, additional breast imaging (with exams such as ultrasound) or a biopsy may be ordered. A biopsy followed by pathological (microscopic) analysis is a definitive way to determine whether a subject has breast cancer. Excised breast cancer samples often are subjected to the following analyses: diagnosis of the breast tumor and confirmation of its malignancy; maximum tumor thickness; assessment of completeness of excision of invasive and *in situ* components and microscopic measurements of the shortest extent of clearance; level of invasion; presence and extent of regression; presence and extent of ulceration; histological type and special variants; pre-existing lesion; mitotic rate; vascular invasion; neurotropism; cell type; tumor lymphocyte infiltration; and growth phase.

[0031] The stage of a breast cancer can be classified as a range of stages from Stage 0 to Stage IV based on its size and the extent to which it has spread. The following table summarizes the stages:

Table A

Stage	Tumor Size	Lymph Node Involvement	Metastasis (Spread)
I	Less than 2 cm	No	No
II	Between 2-5 cm	No or in same side of breast	No
III	More than 5 cm	Yes, on same side of breast	No
IV	Not applicable	Not applicable	Yes

[0032] Stage 0 cancer is a contained cancer that has not spread beyond the breast ductal system. Fifteen to twenty percent of breast cancers detected by clinical examinations or testing are in Stage 0 (the earliest form of breast cancer). Two types of Stage 0 cancer are lobular carcinoma in situ (LCIS) and ductal carcinoma in situ (DCIS). LCIS indicates high risk for breast cancer. Many physicians do not classify LCIS as a malignancy and often encounter LCIS by chance on breast biopsy while investigating another area of concern. While the microscopic features of LCIS are abnormal and are similar to malignancy, LCIS does not behave as a cancer (and therefore is not treated as a cancer). LCIS is merely a marker for a significantly increased risk of cancer anywhere in the breast. However, bilateral simple mastectomy may be occasionally performed if LCIS patients have a strong family

history of breast cancer. In DCIS the cancer cells are confined to milk ducts in the breast and have not spread into the fatty breast tissue or to any other part of the body (such as the lymph nodes). DCIS may be detected on mammogram as tiny specks of calcium (known as microcalcifications) 80% of the time. Less commonly DCIS can present itself as a mass with calcifications (15% of the time); and even less likely as a mass without calcifications (<5% of the time). A breast biopsy is used to confirm DCIS. A standard DCIS treatment is breast-conserving therapy (BCT), which is lumpectomy followed by radiation treatment or mastectomy. To date, DCIS patients have chosen equally among lumpectomy and mastectomy as their treatment option, though specific cases may sometimes favor lumpectomy over mastectomy or vice versa.

[0033] In Stage I, the primary (original) cancer is 2 cm or less in diameter and has not spread to the lymph nodes. In Stage IIA, the primary tumor is between 2 and 5 cm in diameter and has not spread to the lymph nodes. In Stage IIB, the primary tumor is between 2 and 5 cm in diameter and has spread to the axillary (underarm) lymph nodes; or the primary tumor is over 5 cm and has not spread to the lymph nodes. In Stage IIIA, the primary breast cancer of any kind that has spread to the axillary (underarm) lymph nodes and to axillary tissues. In Stage IIIB, the primary breast cancer is any size, has attached itself to the chest wall, and has spread to the pectoral (chest) lymph nodes. In Stage IV, the primary cancer has spread out of the breast to other parts of the body (such as bone, lung, liver, brain). The treatment of Stage IV breast cancer focuses on extending survival time and relieving symptoms.

[0034] Based in part upon selection criteria set forth above, individuals having breast cancer can be selected for genetic studies. Also, individuals having no history of cancer or breast cancer often are selected for genetic studies. Other selection criteria can include: a tissue or fluid sample is derived from an individual characterized as Caucasian; the sample was derived from an individual of German paternal and maternal descent; the database included relevant phenotype information for the individual; case samples were derived from individuals diagnosed with breast cancer; control samples were derived from individuals free of cancer and no family history of breast cancer; and sufficient genomic DNA was extracted from each blood sample for all allelotyping and genotyping reactions performed during the study. Phenotype information included pre- or post-menopausal, familial predisposition, country or origin of mother and father, diagnosis with breast cancer (date of primary diagnosis, age of individual as of primary diagnosis, grade or stage of development, occurrence of metastases, *e.g.*, lymph node metastases, organ metastases), condition of body tissue (skin tissue, breast tissue, ovary tissue, peritoneum tissue and myometrium), method of treatment (surgery, chemotherapy, hormone therapy, radiation therapy).

[0035] Provided herein is a set of blood samples and a set of corresponding nucleic acid samples isolated from the blood samples, where the blood samples are donated from individuals diagnosed with breast cancer. The sample set often includes blood samples or nucleic acid samples from 100 or more, 150 or more, or 200 or more individuals having breast cancer, and sometimes from 250 or

more, 300 or more, 400 or more, or 500 or more individuals. The individuals can have parents from any place of origin, and in an embodiment, the set of samples are extracted from individuals of German paternal and German maternal ancestry. The samples in each set may be selected based upon five or more criteria and/or phenotypes set forth above.

Polymorphic Variants Associated with Breast Cancer

[0036] A genetic analysis provided herein linked breast cancer with polymorphic variants in the *DLG1*, *KIAA0783*, *DPF3* and *CENPC1* regions of the human genome disclosed herein. As used herein, the term “polymorphic site” refers to a region in a nucleic acid at which two or more alternative nucleotide sequences are observed in a significant number of nucleic acid samples from a population of individuals. A polymorphic site may be a nucleotide sequence of two or more nucleotides, an inserted nucleotide or nucleotide sequence, a deleted nucleotide or nucleotide sequence, or a microsatellite, for example. A polymorphic site that is two or more nucleotides in length may be 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 or more, 20 or more, 30 or more, 50 or more, 75 or more, 100 or more, 500 or more, or about 1000 nucleotides in length, where all or some of the nucleotide sequences differ within the region. A polymorphic site is often one nucleotide in length, which is referred to herein as a “single nucleotide polymorphism” or a “SNP.”

[0037] Where there are two, three, or four alternative nucleotide sequences at a polymorphic site, each nucleotide sequence is referred to as a “polymorphic variant” or “nucleic acid variant.” Where two polymorphic variants exist, for example, the polymorphic variant represented in a minority of samples from a population is sometimes referred to as a “minor allele” and the polymorphic variant that is more prevalently represented is sometimes referred to as a “major allele.” Many organisms possess a copy of each chromosome (*e.g.*, humans), and those individuals who possess two major alleles or two minor alleles are often referred to as being “homozygous” with respect to the polymorphism, and those individuals who possess one major allele and one minor allele are normally referred to as being “heterozygous” with respect to the polymorphism. Individuals who are homozygous with respect to one allele are sometimes predisposed to a different phenotype as compared to individuals who are heterozygous or homozygous with respect to another allele.

[0038] Furthermore, a genotype or polymorphic variant may be expressed in terms of a “haplotype,” which as used herein refers to two or more polymorphic variants occurring within genomic DNA in a group of individuals within a population. For example, two SNPs may exist within a gene where each SNP position includes a cytosine variation and an adenine variation. Certain individuals in a population may carry one allele (heterozygous) or two alleles (homozygous) having the gene with a cytosine at each SNP position. As the two cytosines corresponding to each SNP in the gene travel together on one or both alleles in these individuals, the individuals can be characterized as having a cytosine/cytosine haplotype with respect to the two SNPs in the gene.

[0039] As used herein, the term “phenotype” refers to a trait which can be compared between individuals, such as presence or absence of a condition, a visually observable difference in appearance between individuals, metabolic variations, physiological variations, variations in the function of biological molecules, and the like. An example of a phenotype is occurrence of breast cancer.

[0040] Researchers sometimes report a polymorphic variant in a database without determining whether the variant is represented in a significant fraction of a population. Because a subset of these reported polymorphic variants are not represented in a statistically significant portion of the population, some of them are sequencing errors and/or not biologically relevant. Thus, it is often not known whether a reported polymorphic variant is statistically significant or biologically relevant until the presence of the variant is detected in a population of individuals and the frequency of the variant is determined. Methods for detecting a polymorphic variant in a population are described herein, specifically in Example 2. A polymorphic variant is statistically significant and often biologically relevant if it is represented in 5% or more of a population, sometimes 10% or more, 15% or more, or 20% or more of a population, and often 25% or more, 30% or more, 35% or more, 40% or more, 45% or more, or 50% or more of a population.

[0041] A polymorphic variant may be detected on either or both strands of a double-stranded nucleic acid. For example, a thymine at a particular position in SEQ ID NO: 1 can be reported as an adenine from the complementary strand. Also, a polymorphic variant may be located within an intron or exon of a gene or within a portion of a regulatory region such as a promoter, a 5′ untranslated region (UTR), a 3′ UTR, and in DNA (*e.g.*, genomic DNA (gDNA) and complementary DNA (cDNA)), RNA (*e.g.*, mRNA, tRNA, and rRNA), or a polypeptide. Polymorphic variations may or may not result in detectable differences in gene expression, polypeptide structure, or polypeptide function.

[0042] In the genetic analysis that associated breast cancer with the polymorphic variants described hereafter, samples from individuals having breast cancer and individuals not having cancer were allelotyped and genotyped. The term “genotyped” as used herein refers to a process for determining a genotype of one or more individuals, where a “genotype” is a representation of one or more polymorphic variants in a population. Genotypes may be expressed in terms of a “haplotype,” which as used herein refers to two or more polymorphic variants occurring within genomic DNA in a group of individuals within a population. For example, two SNPs may exist within a gene where each SNP position includes a cytosine variation and an adenine variation. Certain individuals in a population may carry one allele (heterozygous) or two alleles (homozygous) having the gene with a cytosine at each SNP position. As the two cytosines corresponding to each SNP in the gene travel together on one or both alleles in these individuals, the individuals can be characterized as having a cytosine/cytosine haplotype with respect to the two SNPs in the gene.

[0043] It was determined that polymorphic variations associated with an increased risk of breast cancer existed in *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleotide sequences. Polymorphic variants

in and around the *DLGI*, *KIAA0783*, *DPF3* and *CENPCI* loci were tested for association with breast cancer. In the *DLGI* locus, these included polymorphic variants at positions in SEQ ID NO: 1 selected from the group consisting of 133, 7938, 8873, 13221, 17288, 25732, 26923, 39977, 41284, 41410, 41477, 41514, 42606, 42742, 59515, 59808, 60265, 67152, 68332, 71128 and 76427.

Polymorphic variants in a region spanning positions 7938-59808 in SEQ ID NO: 1 in particular were associated with an increased risk of breast cancer, including polymorphic variants at positions 7938, 26923, 39977 and 59808 in SEQ ID NO: 1. At these positions in SEQ ID NO: 1, a thymine at position 7938, a cytosine at position 26923, a thymine at position 39977 and a thymine at position 59808 in particular were associated with risk of breast cancer. Also, a glutamine at position 278 in SEQ ID NO: 9 in a *DLGI* polypeptide in particular was associated with an increased risk of breast cancer.

[0044] In the *KIAA0783* locus, these included polymorphic variants at positions in SEQ ID NO: 2 selected from the group consisting of 201, 6395, 8558, 9429, 9809, 10072, 10511, 11556, 16857, 16951, 17027, 17177, 17615, 17950, 18329, 18384, 18561, 18579, 18871, 27152, 27306, 28091, 28661, 29011, 29962, 29969, 30085, 31656, 31685, 31749, 45389, 45459, 46647, 49860, 53061, 57308, 61563, 61660, 62212, 67090, 67198, 70071, 70191, 74006, 75600, 85761, 90798, 90883, 91259, 95416, 95446, 96368, 97050, 97362, 97630, 97989 and 98107. Polymorphic variants in a region spanning positions 10511-98107 in SEQ ID NO: 2 in particular were associated with an increased risk of breast cancer, including polymorphic variants at positions 10511, 11556, 17177, 18384, 28661, 31656, 31685, 31749, 45389, 45459, 46647, 49860, 53061, 57308, 61563, 61660, 67090, 67198, 70071, 74006, 75600, 85761, 90798, 90883, 91259, 95416, 95446, 96368, 97362, 97630, 97989 and 98107 in SEQ ID NO: 2. At these positions in SEQ ID NO: 2, a thymine at position 10511, a cytosine at position 11556, a thymine at position 17177, a thymine at position 18384, an adenine at position 28661, an adenine at position 31656, an adenine at position 31685, a guanine at position 31749, a thymine at position 45389, a guanine at position 45459, an adenine at position 46647, a thymine at position 49860, a thymine at position 53061, an adenine at position 57308, a guanine at position 61563, a guanine at position 61660, a guanine at position 67090, a cytosine at position 67198, an adenine at position 70071, a cytosine at position 74006, an adenine at position 75600, a guanine at position 85761, a thymine at position 90798, a cytosine at position 90883, an adenine at position 91259, a cytosine at position 95416, a thymine at position 95446, a thymine at position 96368, a thymine at position 97362, an adenine at position 97630, a cytosine at position 97989 and a thymine at position 98107 in particular were associated with increased risk of breast cancer.

[0045] In the *DPF3* locus, these included polymorphic variants at positions in SEQ ID NO: 3 selected from the group consisting of 160, 6053, 9719, 10481, 10676, 17179, 18561, 18658, 18694, 18858, 24582, 24683, 24767, 27402, 28150, 28494, 32003, 35588, 35619, 35856, 36254, 37314, 40033, 40095, 42593, 42799, 43090, 46683, 49774, 51796, 52079, 53857, 53971, 55899, 60682,

61291, 72720, 72752, 85507 and 89751. Polymorphic variants in a region spanning positions 160-72752 in SEQ ID NO: 3 in particular were associated with an increased risk of breast cancer, including polymorphic variants at positions 160, 6053, 18658, 18694, 18858, 24683, 27402, 28494, 32003, 35588, 35856, 40095, 46683, 52079, 53857, 72720 and 72752 in SEQ ID NO: 3. At these positions in SEQ ID NO: 3, an adenine at position 160, a guanine at position 6053, a guanine at position 18658, a guanine at position 18694, a thymine at position 18858, a guanine at position 24683, a guanine at position 27402, a thymine at position 28494, an adenine at position 32003, a cytosine at position 35588, an adenine at position 35856, a guanine at position 40095, an adenine at position 46683, an adenine at position 52079, a cytosine at position 53857, an adenine at position 72720 and a cytosine at position 72752 in particular were associated with an increased risk of breast cancer.

[0046] In the *CENPCI* locus, these included polymorphic variants at positions in SEQ ID NO: 4 selected from the group consisting of 196, 13311, 14486, 14691, 15551, 17702, 17872, 19588, 19910, 20006, 20575, 21092, 22830, 23455, 23716, 23890, 24001, 24995, 27282, 27779, 29099, 31185, 33994, 34942, 35137, 36538, 37139, 37358, 38828, 39469, 40233, 40472, 41679, 41682, 42831, 42976, 44128, 44195, 46769, 47363, 48843, 52574, 52602, 53212, 53781, 54710, 55808, 57987, 58556, 59148, 59286, 60217, 60412, 60753, 60791, 61524, 62543, 62825, 62826, 62857, 63400, 63960, 64307, 64539, 65728, 66000, 66521, 68185, 69643, 74909, 82973, 83039, 85713, 86873, 90293, 91810, 92609, 92884 and 42831. Polymorphic variants in a region spanning positions 196-74909 in SEQ ID NO: 4 in particular were associated with an increased risk of breast cancer, including polymorphic variants at positions 196, 13311, 14486, 19910, 20575, 23716, 23890, 24995, 29099, 33994, 34942, 37139, 40233, 40472, 42831, 42976, 44195, 48843, 58556, 59286, 60217, 62826, 62857, 63400, 63960 and 74909 in SEQ ID NO: 4. At these positions in SEQ ID NO: 4, an adenine at position 196, a guanine at position 13311, a thymine at position 14486, a thymine at position 19910, an adenine at position 20575, a guanine at position 23716, a guanine at position 23890, an adenine at position 24995, a cytosine at position 29099, a thymine at position 33994, a thymine at position 34942, a thymine at position 37139, a thymine at position 40233, an adenine at position 40472, a guanine at position 42831, a guanine at position 42976, a thymine at position 44195, a thymine at position 48843, an adenine at position 58556, a guanine at position 59286, an adenine at position 60217, a cytosine at position 62826, a thymine at position 62857, a thymine at position 63400, an adenine at position 63960 and a cytosine at position 74909 in particular were associated with an increased risk of breast cancer. Also, a glycine at position 389 in SEQ ID NO: 12 in a *CENPCI* polypeptide in particular was associated with an increased risk of breast cancer.

Additional Polymorphic Variants Associated with Breast Cancer

[0047] Also provided is a method for identifying polymorphic variants proximal to an incident, founder polymorphic variant associated with breast cancer. Thus, featured herein are methods for identifying a polymorphic variation associated with breast cancer that is proximal to an incident

polymorphic variation associated with breast cancer, which comprises identifying a polymorphic variant proximal to the incident polymorphic variant associated with breast cancer, where the incident polymorphic variant is in a nucleotide sequence set forth in SEQ ID NO: 1-4. The nucleotide sequence often comprises a polynucleotide sequence selected from the group consisting of (a) a nucleotide sequence set forth in SEQ ID NO: 1-4; (b) a nucleotide sequence which encodes a polypeptide having an amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-4; (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to an amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-4 or a nucleotide sequence about 90% or more identical to the nucleotide sequence set forth in SEQ ID NO: 1-4; and (d) a fragment of a nucleotide sequence of (a), (b), or (c), often a fragment that includes a polymorphic site associated with breast cancer. The presence or absence of an association of the proximal polymorphic variant with breast cancer then is determined using a known association method, such as a method described in the Examples hereafter. In an embodiment, the incident polymorphic variant is described in SEQ ID NO: 1-4. In another embodiment, the proximal polymorphic variant identified sometimes is a publicly disclosed polymorphic variant, which for example, sometimes is published in a publicly available database. In other embodiments, the polymorphic variant identified is not publicly disclosed and is discovered using a known method, including, but not limited to, sequencing a region surrounding the incident polymorphic variant in a group of nucleic acid samples. Thus, multiple polymorphic variants proximal to an incident polymorphic variant are associated with breast cancer using this method.

[0048] The proximal polymorphic variant often is identified in a region surrounding the incident polymorphic variant. In certain embodiments, this surrounding region is about 50 kb flanking the first polymorphic variant (*e.g.* about 50 kb 5' of the first polymorphic variant and about 50 kb 3' of the first polymorphic variant), and the region sometimes is composed of shorter flanking sequences, such as flanking sequences of about 40 kb, about 30 kb, about 25 kb, about 20 kb, about 15 kb, about 10 kb, about 7 kb, about 5 kb, or about 2 kb 5' and 3' of the incident polymorphic variant. In other embodiments, the region is composed of longer flanking sequences, such as flanking sequences of about 55 kb, about 60 kb, about 65 kb, about 70 kb, about 75 kb, about 80 kb, about 85 kb, about 90 kb, about 95 kb, or about 100 kb 5' and 3' of the incident polymorphic variant.

[0049] In certain embodiments, polymorphic variants associated with breast cancer are identified iteratively. For example, a first proximal polymorphic variant is associated with breast cancer using the methods described above and then another polymorphic variant proximal to the first proximal polymorphic variant is identified (*e.g.*, publicly disclosed or discovered) and the presence or absence of an association of one or more other polymorphic variants proximal to the first proximal polymorphic variant with breast cancer is determined.

[0050] The methods described herein are useful for identifying or discovering additional polymorphic variants that may be used to further characterize a gene, region or loci associated with a

condition, a disease (*e.g.*, breast cancer), or a disorder. For example, allelotyping or genotyping data from the additional polymorphic variants may be used to identify a functional mutation or a region of linkage disequilibrium.

[0051] In certain embodiments, polymorphic variants identified or discovered within a region comprising the first polymorphic variant associated with breast cancer are genotyped using the genetic methods and sample selection techniques described herein, and it can be determined whether those polymorphic variants are in linkage disequilibrium with the first polymorphic variant. The size of the region in linkage disequilibrium with the first polymorphic variant also can be assessed using these genotyping methods. Thus, provided herein are methods for determining whether a polymorphic variant is in linkage disequilibrium with a first polymorphic variant associated with breast cancer, and such information can be used in prognosis methods described herein.

Isolated *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* Nucleic Acids

[0052] Featured herein are isolated *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acids, which include the nucleic acid having the nucleotide sequence of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or 11, nucleic acid variants, and substantially identical nucleic acids of the foregoing. Nucleotide sequences of the *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acids sometimes are referred to herein as “*DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleotide sequences.” A “*DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acid variant” refers to one allele that may have one or more different polymorphic variations as compared to another allele in another subject or the same subject. A polymorphic variation in the *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acid variant may be represented on one or both strands in a double-stranded nucleic acid or on one chromosomal complement (heterozygous) or both chromosomal complements (homozygous).

[0053] As used herein, the term “nucleic acid” includes DNA molecules (*e.g.*, a complementary DNA (cDNA) and genomic DNA (gDNA)) and RNA molecules (*e.g.*, mRNA, rRNA, and tRNA) and analogs of DNA or RNA, for example, by use of nucleotide analogs. The nucleic acid molecule can be single-stranded and it is often double-stranded. The term “isolated or purified nucleic acid” refers to nucleic acids that are separated from other nucleic acids present in the natural source of the nucleic acid. For example, with regard to genomic DNA, the term “isolated” includes nucleic acids which are separated from the chromosome with which the genomic DNA is naturally associated. An “isolated” nucleic acid is often free of sequences which naturally flank the nucleic acid (*i.e.*, sequences located at the 5’ and/or 3’ ends of the nucleic acid) in the genomic DNA of the organism from which the nucleic acid is derived. For example, in various embodiments, the isolated nucleic acid molecule can contain less than about 5 kb, 4 kb, 3 kb, 2 kb, 1 kb, 0.5 kb or 0.1 kb of 5’ and/or 3’ nucleotide sequences which flank the nucleic acid molecule in genomic DNA of the cell from which the nucleic acid is derived. Moreover, an “isolated” nucleic acid molecule, such as a cDNA molecule, can be substantially free of other cellular material, or culture medium when produced by recombinant

techniques, or substantially free of chemical precursors or other chemicals when chemically synthesized. As used herein, the term “*DLG1*, *KIAA0783*, *DPF3* or *CENPC1* gene” refers to a nucleotide sequence that encodes a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide.

[0054] Also included herein are nucleic acid fragments. These fragments typically are a nucleotide sequence identical to a nucleotide sequence in SEQ ID NO: 1-8, a nucleotide sequence substantially identical to a nucleotide sequence in SEQ ID NO: 1-8, or a nucleotide sequence that is complementary to the foregoing. The nucleic acid fragment may be identical, substantially identical or homologous to a nucleotide sequence in an exon or an intron in SEQ ID NO: 1-4, and may encode a domain or part of a domain or motif of a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide, sometimes the domains set forth in Figures 13-18. Sometimes, the fragment comprises the polymorphic variation described herein as being associated with breast cancer. The nucleic acid fragment sometimes is 50, 100, or 200 or fewer base pairs in length, and is sometimes about 300, 400, 500, 600, 700, 800, 900, 1000, 1100, 1200, 1300, 1400, 1500, 1600, 1700, 1800, 1900, 2000, 2100, 2200, 2300, 2400, 2500, 2600, 2700, 2800, 2900, 3000, 3100, 3200, 3300, 3400, 3500, 3600, 3800, 4000, 5000, 6000, 7000, 8000, 9000, 10000, 15000, 20000, 30000, 40000, 50000, 60000, 70000, 80000, 90000, 100000, 110000, 120000, 130000, 140000, 150000 or 160000 base pairs in length. A nucleic acid fragment complementary to a nucleotide sequence identical or substantially identical to the nucleotide sequence of SEQ ID NO: 1-8 and hybridizes to such a nucleotide sequence under stringent conditions often is referred to as a “probe.” Nucleic acid fragments often include one or more polymorphic sites, or sometimes have an end that is adjacent to a polymorphic site as described hereafter.

[0055] An example of a nucleic acid fragment is an oligonucleotide. As used herein, the term “oligonucleotide” refers to a nucleic acid comprising about 8 to about 50 covalently linked nucleotides, often comprising from about 8 to about 35 nucleotides, and more often from about 10 to about 25 nucleotides. The backbone and nucleotides within an oligonucleotide may be the same as those of naturally occurring nucleic acids, or analogs or derivatives of naturally occurring nucleic acids, provided that oligonucleotides having such analogs or derivatives retain the ability to hybridize specifically to a nucleic acid comprising a targeted polymorphism. Oligonucleotides described herein may be used as hybridization probes or as components of prognostic or diagnostic assays, for example, as described herein.

[0056] Oligonucleotides are typically synthesized using standard methods and equipment, such as the ABI 3900 High Throughput DNA Synthesizer and the EXPEDITE™ 8909 Nucleic Acid Synthesizer, both of which are available from Applied Biosystems (Foster City, CA). Analogs and derivatives are exemplified in U.S. Pat. Nos. 4,469,863; 5,536,821; 5,541,306; 5,637,683; 5,637,684; 5,700,922; 5,717,083; 5,719,262; 5,739,308; 5,773,601; 5,886,165; 5,929,226; 5,977,296; 6,140,482; WO 00/56746; WO 01/14398, and related publications. Methods for synthesizing oligonucleotides comprising such analogs or derivatives are disclosed, for example, in the patent publications cited

above and in U.S. Pat. Nos. 5,614,622; 5,739,314; 5,955,599; 5,962,674; 6,117,992; in WO 00/75372; and in related publications.

[0057] Oligonucleotides also may be linked to a second moiety. The second moiety may be an additional nucleotide sequence such as a tail sequence (e.g., a polyadenosine tail), an adapter sequence (e.g., phage M13 universal tail sequence), and others. Alternatively, the second moiety may be a non-nucleotide moiety such as a moiety which facilitates linkage to a solid support or a label to facilitate detection of the oligonucleotide. Such labels include, without limitation, a radioactive label, a fluorescent label, a chemiluminescent label, a paramagnetic label, and the like. The second moiety may be attached to any position of the oligonucleotide, provided the oligonucleotide can hybridize to the nucleic acid comprising the polymorphism.

Uses for Nucleic Acid Sequences

[0058] Nucleic acid coding sequences depicted in SEQ ID NO: 1-8 may be used for diagnostic purposes for detection and control of polypeptide expression. Also, included herein are oligonucleotide sequences such as antisense RNA, small-interfering RNA (siRNA) and DNA molecules and ribozymes that function to inhibit translation of a polypeptide. Antisense techniques and RNA interference techniques are known in the art and are described herein.

[0059] Ribozymes are enzymatic RNA molecules capable of catalyzing the specific cleavage of RNA. The mechanism of ribozyme action involves sequence specific hybridization of the ribozyme molecule to complementary target RNA, followed by an endonucleolytic cleavage. Ribozymes may be engineered hammerhead motif ribozyme molecules that specifically and efficiently catalyze endonucleolytic cleavage of RNA sequences corresponding to or complementary to the nucleotide sequences set forth in SEQ ID NO: 1-8. Specific ribozyme cleavage sites within any potential RNA target are initially identified by scanning the target molecule for ribozyme cleavage sites which include the following sequences, GUA, GUU and GUC. Once identified, short RNA sequences of between fifteen (15) and twenty (20) ribonucleotides corresponding to the region of the target gene containing the cleavage site may be evaluated for predicted structural features such as secondary structure that may render the oligonucleotide sequence unsuitable. The suitability of candidate targets may also be evaluated by testing their accessibility to hybridization with complementary oligonucleotides, using ribonuclease protection assays.

[0060] Antisense RNA and DNA molecules, siRNA and ribozymes may be prepared by any method known in the art for the synthesis of RNA molecules. These include techniques for chemically synthesizing oligodeoxyribonucleotides well known in the art such as solid phase phosphoramidite chemical synthesis. Alternatively, RNA molecules may be generated by *in vitro* and *in vivo* transcription of DNA sequences encoding the antisense RNA molecule. Such DNA sequences may be incorporated into a wide variety of vectors which incorporate suitable RNA polymerase promoters such as the T7 or SP6 polymerase promoters. Alternatively, antisense cDNA constructs

that synthesize antisense RNA constitutively or inducibly, depending on the promoter used, can be introduced stably into cell lines.

[0061] DNA encoding a polypeptide also may have a number of uses for the diagnosis of diseases, including breast cancer, resulting from aberrant expression of a target gene described herein. For example, the nucleic acid sequence may be used in hybridization assays of biopsies or autopsies to diagnose abnormalities of expression or function (e.g., Southern or Northern blot analysis, in situ hybridization assays).

[0062] In addition, the expression of a polypeptide during embryonic development may also be determined using nucleic acid encoding the polypeptide. As addressed, *infra*, production of functionally impaired polypeptide can be the cause of various disease states, such as breast cancer. *In situ* hybridizations using polynucleotide probes may be employed to predict problems related to breast cancer. Further, as indicated, *infra*, administration of human active polypeptide, recombinantly produced as described herein, may be used to treat disease states related to functionally impaired polypeptide. Alternatively, gene therapy approaches may be employed to remedy deficiencies of functional polypeptide or to replace or compete with dysfunctional polypeptide.

Expression Vectors, Host Cells, and Genetically Engineered Cells

[0063] Provided herein are nucleic acid vectors, often expression vectors, which contain a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acid. As used herein, the term “vector” refers to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked and can include a plasmid, cosmid, or viral vector. The vector can be capable of autonomous replication or it can integrate into a host DNA. Viral vectors may include replication defective retroviruses, adenoviruses and adeno-associated viruses for example.

[0064] A vector can include a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acid in a form suitable for expression of the nucleic acid in a host cell. The recombinant expression vector typically includes one or more regulatory sequences operatively linked to the nucleic acid sequence to be expressed. The term “regulatory sequence” includes promoters, enhancers and other expression control elements (e.g., polyadenylation signals). Regulatory sequences include those that direct constitutive expression of a nucleotide sequence, as well as tissue-specific regulatory and/or inducible sequences. The design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of polypeptide desired, and the like. Expression vectors can be introduced into host cells to produce *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptides, including fusion polypeptides, encoded by *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acids.

[0065] Recombinant expression vectors can be designed for expression of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptides in prokaryotic or eukaryotic cells. For example, *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptides can be expressed in *E. coli*, insect cells (e.g., using baculovirus expression vectors), yeast cells, or mammalian cells. Suitable host cells are discussed further in

Goeddel, Gene Expression Technology: Methods in Enzymology 185, Academic Press, San Diego, CA (1990). Alternatively, the recombinant expression vector can be transcribed and translated in vitro, for example using T7 promoter regulatory sequences and T7 polymerase.

[0066] Expression of polypeptides in prokaryotes is most often carried out in *E. coli* with vectors containing constitutive or inducible promoters directing the expression of either fusion or non-fusion polypeptides. Fusion vectors add a number of amino acids to a polypeptide encoded therein, usually to the amino terminus of the recombinant polypeptide. Such fusion vectors typically serve three purposes: 1) to increase expression of recombinant polypeptide; 2) to increase the solubility of the recombinant polypeptide; and 3) to aid in the purification of the recombinant polypeptide by acting as a ligand in affinity purification. Often, a proteolytic cleavage site is introduced at the junction of the fusion moiety and the recombinant polypeptide to enable separation of the recombinant polypeptide from the fusion moiety subsequent to purification of the fusion polypeptide. Such enzymes, and their cognate recognition sequences, include Factor Xa, thrombin and enterokinase. Typical fusion expression vectors include pGEX (Pharmacia Biotech Inc; Smith & Johnson, Gene 67: 31-40 (1988)), pMAL (New England Biolabs, Beverly, MA) and pRIT5 (Pharmacia, Piscataway, NJ) which fuse glutathione S-transferase (GST), maltose E binding polypeptide, or polypeptide A, respectively, to the target recombinant polypeptide.

[0067] Purified fusion polypeptides can be used in screening assays and to generate antibodies specific for *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptides. In a therapeutic embodiment, fusion polypeptide expressed in a retroviral expression vector is used to infect bone marrow cells that are subsequently transplanted into irradiated recipients. The pathology of the subject recipient is then examined after sufficient time has passed (e.g., six (6) weeks).

[0068] Expressing the polypeptide in host bacteria with an impaired capacity to proteolytically cleave the recombinant polypeptide is often used to maximize recombinant polypeptide expression (Gottesman, S., Gene Expression Technology: Methods in Enzymology, Academic Press, San Diego, California 185: 119-128 (1990)). Another strategy is to alter the nucleotide sequence of the nucleic acid to be inserted into an expression vector so that the individual codons for each amino acid are those preferentially utilized in *E. coli* (Wada et al., Nucleic Acids Res. 20: 2111-2118 (1992)). Such alteration of nucleotide sequences can be carried out by standard DNA synthesis techniques.

[0069] When used in mammalian cells, the expression vector's control functions are often provided by viral regulatory elements. For example, commonly used promoters are derived from polyoma, Adenovirus 2, cytomegalovirus and Simian Virus 40. Recombinant mammalian expression vectors are often capable of directing expression of the nucleic acid in a particular cell type (e.g., tissue-specific regulatory elements are used to express the nucleic acid). Non-limiting examples of suitable tissue-specific promoters include an albumin promoter (liver-specific; Pinkert et al., Genes Dev. 1: 268-277 (1987)), lymphoid-specific promoters (Calame & Eaton, Adv. Immunol. 43: 235-275 (1988)), promoters of T cell receptors (Winoto & Baltimore, EMBO J. 8: 729-733 (1989))

promoters of immunoglobulins (Banerji et al., Cell 33: 729-740 (1983); Queen & Baltimore, Cell 33: 741-748 (1983)), neuron-specific promoters (e.g., the neurofilament promoter; Byrne & Ruddle, Proc. Natl. Acad. Sci. USA 86: 5473-5477 (1989)), pancreas-specific promoters (Edlund et al., Science 230: 912-916 (1985)), and mammary gland-specific promoters (e.g., milk whey promoter; U.S. Patent No. 4,873,316 and European Application Publication No. 264,166). Developmentally-regulated promoters are sometimes utilized, for example, the murine hox promoters (Kessel & Gruss, Science 249: 374-379 (1990)) and the α -fetopolypeptide promoter (Campes & Tilghman, Genes Dev. 3: 537-546 (1989)).

[0070] A *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acid may also be cloned into an expression vector in an antisense orientation. Regulatory sequences (e.g., viral promoters and/or enhancers) operatively linked to a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acid cloned in the antisense orientation can be chosen for directing constitutive, tissue specific or cell type specific expression of antisense RNA in a variety of cell types. Antisense expression vectors can be in the form of a recombinant plasmid, phagemid or attenuated virus. For a discussion of the regulation of gene expression using antisense genes see Weintraub et al., Antisense RNA as a molecular tool for genetic analysis, Reviews - Trends in Genetics, Vol. 1(1) (1986).

[0071] Also provided herein are host cells that include a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acid within a recombinant expression vector or *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acid sequence fragments which allow it to homologously recombine into a specific site of the host cell genome. The terms "host cell" and "recombinant host cell" are used interchangeably herein. Such terms refer not only to the particular subject cell but rather also to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein. A host cell can be any prokaryotic or eukaryotic cell. For example, a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide can be expressed in bacterial cells such as *E. coli*, insect cells, yeast or mammalian cells (such as Chinese hamster ovary cells (CHO) or COS cells). Other suitable host cells are known to those skilled in the art.

[0072] Vectors can be introduced into host cells via conventional transformation or transfection techniques. As used herein, the terms "transformation" and "transfection" are intended to refer to a variety of art-recognized techniques for introducing foreign nucleic acid (e.g., DNA) into a host cell, including calcium phosphate or calcium chloride co-precipitation, transduction/infection, DEAE-dextran-mediated transfection, lipofection, or electroporation.

[0073] A host cell provided herein can be used to produce (i.e., express) a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide. Accordingly, further provided are methods for producing a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide using the host cells described herein. In one embodiment, the method includes culturing host cells into which a recombinant expression vector encoding a

DLG1, *KIAA0783*, *DPF3* or *CENPC1* polypeptide has been introduced in a suitable medium such that a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide is produced. In another embodiment, the method further includes isolating a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide from the medium or the host cell.

[0074] Also provided are cells or purified preparations of cells which include a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* transgene, or which otherwise misexpress *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide. Cell preparations can consist of human or non-human cells, e.g., rodent cells, e.g., mouse or rat cells, rabbit cells, or pig cells. In certain embodiments, the cell or cells include a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* transgene (e.g., a heterologous form of a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* such as a human gene expressed in non-human cells). The *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* transgene can be misexpressed, e.g., overexpressed or underexpressed. In other embodiments, the cell or cells include a gene which misexpress an endogenous *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide (e.g., expression of a gene is disrupted, also known as a knockout). Such cells can serve as a model for studying disorders which are related to mutated or mis-expressed *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* alleles or for use in drug screening. Also provided are human cells (e.g., a hematopoietic stem cells) transformed with a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acid.

[0075] Also provided are cells or a purified preparation thereof (e.g., human cells) in which an endogenous *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acid is under the control of a regulatory sequence that does not normally control the expression of the endogenous *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* gene. The expression characteristics of an endogenous gene within a cell (e.g., a cell line or microorganism) can be modified by inserting a heterologous DNA regulatory element into the genome of the cell such that the inserted regulatory element is operably linked to the endogenous *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* gene. For example, an endogenous *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* gene (e.g., a gene which is “transcriptionally silent,” not normally expressed, or expressed only at very low levels) may be activated by inserting a regulatory element which is capable of promoting the expression of a normally expressed gene product in that cell. Techniques such as targeted homologous recombinations, can be used to insert the heterologous DNA as described in, e.g., Chappel, US 5,272,071; WO 91/06667, published on May 16, 1991.

Transgenic Animals

[0076] Non-human transgenic animals that express a heterologous *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide (e.g., expressed from a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acid isolated from another organism) can be generated. Such animals are useful for studying the function and/or activity of a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide and for identifying and/or evaluating modulators of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acid and *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide activity. As used herein, a “transgenic animal” is a non-human animal

such as a mammal (e.g., a non-human primate such as chimpanzee, baboon, or macaque; an ungulate such as an equine, bovine, or caprine; or a rodent such as a rat, a mouse, or an Israeli sand rat), a bird (e.g., a chicken or a turkey), an amphibian (e.g., a frog, salamander, or newt), or an insect (e.g., *Drosophila melanogaster*), in which one or more of the cells of the animal includes a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* transgene. A transgene is exogenous DNA or a rearrangement (e.g., a deletion of endogenous chromosomal DNA) that is often integrated into or occurs in the genome of cells in a transgenic animal. A transgene can direct expression of an encoded gene product in one or more cell types or tissues of the transgenic animal, and other transgenes can reduce expression (e.g., a knockout). Thus, a transgenic animal can be one in which an endogenous *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* gene has been altered by homologous recombination between the endogenous gene and an exogenous DNA molecule introduced into a cell of the animal (e.g., an embryonic cell of the animal) prior to development of the animal.

[0077] Intronic sequences and polyadenylation signals can also be included in the transgene to increase expression efficiency of the transgene. One or more tissue-specific regulatory sequences can be operably linked to a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* transgene to direct expression of a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide to particular cells. A transgenic founder animal can be identified based upon the presence of a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* transgene in its genome and/or expression of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* mRNA in tissues or cells of the animals. A transgenic founder animal can then be used to breed additional animals carrying the transgene. Moreover, transgenic animals carrying a transgene encoding a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide can further be bred to other transgenic animals carrying other transgenes.

[0078] *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptides can be expressed in transgenic animals or plants by introducing, for example, a nucleic acid encoding the polypeptide into the genome of an animal. In certain embodiments the nucleic acid is placed under the control of a tissue specific promoter, e.g., a milk or egg specific promoter, and recovered from the milk or eggs produced by the animal. Also included is a population of cells from a transgenic animal.

DLG1, *KIAA0783*, *DPF3* and *CENPC1* Polypeptides

[0079] Featured herein are isolated *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptides, which include polypeptides having amino acid sequences set forth in SEQ ID NO: 9-12, and substantially identical polypeptides thereof. Such polypeptides sometimes are proteins or peptides. A *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide is a polypeptide encoded by a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acid, where one nucleic acid can encode one or more different polypeptides. An "isolated" or "purified" polypeptide or protein is substantially free of cellular material or other contaminating proteins from the cell or tissue source from which the protein is derived, or substantially free from chemical precursors or other chemicals when chemically synthesized. In one embodiment, the language "substantially free" means preparation of a *DLG1*, *KIAA0783*, *DPF3* or

CENPC1 polypeptide or *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide variant having less than about 30%, 20%, 10% and sometimes 5% (by dry weight), of non-*DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide (also referred to herein as a “contaminating protein”), or of chemical precursors or non-*DLG1*, *KIAA0783*, *DPF3* or *CENPC1* chemicals. When the *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide or a biologically active portion thereof is recombinantly produced, it is also often substantially free of culture medium, specifically, where culture medium represents less than about 20%, sometimes less than about 10%, and often less than about 5% of the volume of the polypeptide preparation. Isolated or purified *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide preparations are sometimes 0.01 milligrams or more or 0.1 milligrams or more, and often 1.0 milligrams or more and 10 milligrams or more in dry weight. In specific embodiments, a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide comprises a glutamine at amino acid position 278 in SEQ ID NO: 9 or a glycine at amino acid position 389 in SEQ ID NO: 12.

[0080] In another aspect, featured herein are *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptides and biologically active or antigenic fragments thereof that are useful as reagents or targets in assays applicable to prevention, treatment or diagnosis of breast cancer. In another embodiment, provided herein are *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptides having a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* activity or activities.

[0081] Further included herein are *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide fragments. The polypeptide fragment may be a domain or part of a domain of a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide. The polypeptide fragment is often 50 or fewer, 100 or fewer, or 200 or fewer amino acids in length, and is sometimes 300, 400, 500, 600, 700, or 900 or fewer amino acids in length. In certain embodiments, the polypeptide fragment comprises, consists essentially of, or consists of, at least 6 consecutive amino acids and not more than 1211 consecutive amino acids of SEQ ID NO: 9-12, or the polypeptide fragment comprises, consists essentially of, or consists of, at least 6 consecutive amino acids and not more than 543 consecutive amino acids of SEQ ID NO: 9-12.

[0082] *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptides described herein can be used as immunogens to produce anti-*DLG1*, *KIAA0783*, *DPF3* or *CENPC1* antibodies in a subject, to purify *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* ligands or binding partners, and in screening assays to identify molecules which inhibit or enhance the interaction of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* with a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* substrate. Full-length *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptides and polynucleotides encoding the same may be specifically substituted for a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide fragment or polynucleotide encoding the same in any embodiment described herein.

[0083] Substantially identical polypeptides may depart from the amino acid sequences set forth in SEQ ID NO: 9-12 in different manners. For example, conservative amino acid modifications may be introduced at one or more positions in the amino acid sequences of SEQ ID NO: 9-12. A “conservative amino acid substitution” is one in which the amino acid is replaced by another amino

acid having a similar structure and/or chemical function. Families of amino acid residues having similar structures and functions are well known. These families include amino acids with basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (e.g., alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine). Also, essential and non-essential amino acids may be replaced. A “non-essential” amino acid is one that can be altered without abolishing or substantially altering the biological function of a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide, whereas altering an “essential” amino acid abolishes or substantially alters the biological function of a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide. Amino acids that are conserved among *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptides are typically essential amino acids.

[0084] Also, *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptides and polypeptide variants may exist as chimeric or fusion polypeptides. As used herein, a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* “chimeric polypeptide” or “fusion polypeptide” includes a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide linked to a non-*DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide. A “non-*DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide” refers to a polypeptide having an amino acid sequence corresponding to a polypeptide which is not substantially identical to the *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide, which includes, for example, a polypeptide that is different from the *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide and derived from the same or a different organism. The *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide in the fusion polypeptide can correspond to an entire or nearly entire *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide or a fragment thereof. The non-*DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide can be fused to the N-terminus or C-terminus of the *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide.

[0085] Fusion polypeptides can include a moiety having high affinity for a ligand. For example, the fusion polypeptide can be a GST-*DLG1*, *KIAA0783*, *DPF3* or *CENPC1* fusion polypeptide in which the *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* sequences are fused to the C-terminus of the GST sequences, or a polyhistidine-*DLG1*, *KIAA0783*, *DPF3* or *CENPC1* fusion polypeptide in which the *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide is fused at the N- or C-terminus to a string of histidine residues. Such fusion polypeptides can facilitate purification of recombinant *DLG1*, *KIAA0783*, *DPF3* or *CENPC1*. Expression vectors are commercially available that already encode a fusion moiety (e.g., a GST polypeptide), and a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acid can be cloned into an expression vector such that the fusion moiety is linked in-frame to the *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide. Further, the fusion polypeptide can be a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide containing a heterologous signal sequence at its N-terminus. In certain host cells (e.g., mammalian host cells), expression, secretion, cellular internalization, and cellular localization of a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide can be

increased through use of a heterologous signal sequence. Fusion polypeptides can also include all or a part of a serum polypeptide (e.g., an IgG constant region or human serum albumin).

[0086] *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptides or fragments thereof can be incorporated into pharmaceutical compositions and administered to a subject in vivo. Administration of these *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptides can be used to affect the bioavailability of a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* substrate and may effectively increase or decrease *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* biological activity in a cell or effectively supplement dysfunctional or hyperactive *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide. *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* fusion polypeptides may be useful therapeutically for the treatment of disorders caused by, for example, (i) aberrant modification or mutation of a gene encoding a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide; (ii) mis-regulation of the *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* gene; and (iii) aberrant post-translational modification of a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide. Also, *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptides can be used as immunogens to produce anti-*DLG1*, *KIAA0783*, *DPF3* or *CENPC1* antibodies in a subject, to purify *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* ligands or binding partners, and in screening assays to identify molecules which inhibit or enhance the interaction of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* with a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* substrate. Preferably, said *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptides are used in screening assays to identify molecules which inhibit the interaction of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1*.

[0087] In addition, polypeptides can be chemically synthesized using techniques known in the art (See, e.g., Creighton, 1983 *Proteins*. New York, N.Y.: W. H. Freeman and Company; and Hunkapiller *et al.*, (1984) *Nature* July 12 -18;310(5973):105-11). For example, a relative short polypeptide fragment can be synthesized by use of a peptide synthesizer. Furthermore, if desired, non-classical amino acids or chemical amino acid analogs can be introduced as a substitution or addition into the fragment sequence. Non-classical amino acids include, but are not limited to, to the D-isomers of the common amino acids, 2,4-diaminobutyric acid, α -amino isobutyric acid, 4-aminobutyric acid, Abu, 2-amino butyric acid, g-Abu, e-Ahx, 6-amino hexanoic acid, Aib, 2-amino isobutyric acid, 3-amino propionic acid, ornithine, norleucine, norvaline, hydroxyproline, sarcosine, citrulline, homocitrulline, cysteic acid, t-butylglycine, t-butylalanine, phenylglycine, cyclohexylalanine, b-alanine, fluoroamino acids, designer amino acids such as b-methyl amino acids, Ca-methyl amino acids, Na-methyl amino acids, and amino acid analogs in general. Furthermore, the amino acid can be D (dextrorotary) or L (levorotary).

[0088] Also included are polypeptide fragments which are differentially modified during or after translation, e.g., by glycosylation, acetylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to an antibody molecule or other cellular ligand, and the like. Any of numerous chemical modifications may be carried out by known techniques, including but not limited, to specific chemical cleavage by cyanogen bromide, trypsin,

chymotrypsin, papain, V8 protease, NaBH_4 ; acetylation, formylation, oxidation, reduction; metabolic synthesis in the presence of tunicamycin; and the like.

[0089] Additional post-translational modifications include, for example, N-linked or O-linked carbohydrate chains, processing of N-terminal or C-terminal ends), attachment of chemical moieties to the amino acid backbone, chemical modifications of N-linked or O-linked carbohydrate chains, and addition or deletion of an N-terminal methionine residue as a result of prokaryotic host cell expression. The polypeptide fragments may also be modified with a detectable label, such as an enzymatic, fluorescent, isotopic or affinity label to allow for detection and isolation of the polypeptide.

[0090] Also provided are chemically modified polypeptide derivatives that may provide additional advantages such as increased solubility, stability and circulating time of the polypeptide, or decreased immunogenicity. See U.S. Pat. No: 4,179,337. The chemical moieties for derivitization may be selected from water soluble polymers such as polyethylene glycol, ethylene glycol/propylene glycol copolymers, carboxymethylcellulose, dextran, polyvinyl alcohol and the like. The polypeptides may be modified at random positions within the molecule, or at predetermined positions within the molecule and may include one, two, three or more attached chemical moieties.

[0091] The polymer may be of any molecular weight, and may be branched or unbranched. For polyethylene glycol, the molecular weight is between about 1 kDa and about 100 kDa (the term "about" indicating that in preparations of polyethylene glycol, some molecules will weigh more, some less, than the stated molecular weight) for ease in handling and manufacturing. Other sizes may be used, depending on the desired therapeutic profile (*e.g.*, the duration of sustained release desired, the effects, if any on biological activity, the ease in handling, the degree or lack of antigenicity and other known effects of the polyethylene glycol to a therapeutic protein or analog).

[0092] The polyethylene glycol molecules (or other chemical moieties) should be attached to the polypeptide with consideration of effects on functional or antigenic domains of the polypeptide. There are a number of attachment methods available to those skilled in the art, *e.g.*, EP 0 401 384, herein incorporated by reference (coupling PEG to G-CSF), see also Malik *et al.* (1992) *Exp Hematol.* September;20(8):1028-35, reporting pegylation of GM-CSF using tresyl chloride). For example, polyethylene glycol may be covalently bound through amino acid residues via a reactive group, such as, a free amino or carboxyl group. Reactive groups are those to which an activated polyethylene glycol molecule may be bound. The amino acid residues having a free amino group may include lysine residues and the N-terminal amino acid residues; those having a free carboxyl group may include aspartic acid residues, glutamic acid residues and the C-terminal amino acid residue. Sulfhydryl groups may also be used as a reactive group for attaching the polyethylene glycol molecules. A polymer sometimes is attached at an amino group, such as attachment at the N-terminus or lysine group.

[0093] One may specifically desire proteins chemically modified at the N-terminus. Using polyethylene glycol as an illustration of the present composition, one may select from a variety of polyethylene glycol molecules (by molecular weight, branching, and the like), the proportion of polyethylene glycol molecules to protein (polypeptide) molecules in the reaction mix, the type of pegylation reaction to be performed, and the method of obtaining the selected N-terminally pegylated protein. The method of obtaining the N-terminally pegylated preparation (i.e., separating this moiety from other monopegylated moieties if necessary) may be by purification of the N-terminally pegylated material from a population of pegylated protein molecules. Selective proteins chemically modified at the N-terminus may be accomplished by reductive alkylation, which exploits differential reactivity of different types of primary amino groups (lysine versus the N-terminal) available for derivatization in a particular protein. Under the appropriate reaction conditions, substantially selective derivatization of the protein at the N-terminus with a carbonyl group containing polymer is achieved.

Substantially Identical Nucleic Acids and Polypeptides

[0094] Nucleotide sequences and polypeptide sequences that are substantially identical to a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleotide sequence and the *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide sequences encoded by those nucleotide sequences are included herein. The term “substantially identical” as used herein refers to two or more nucleic acids or polypeptides sharing one or more identical nucleotide sequences or polypeptide sequences, respectively. Included are nucleotide sequences or polypeptide sequences that are 55% or more, 60% or more, 65% or more, 70% or more, 75% or more, 80% or more, 85% or more, 90% or more, 95% or more (each often within a 1%, 2%, 3% or 4% variability) or more identical to the nucleotide sequences in SEQ ID NO: 1-8 or the encoded *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide amino acid sequences. One test for determining whether two nucleic acids are substantially identical is to determine the percent of identical nucleotide sequences or polypeptide sequences shared between the nucleic acids or polypeptides.

[0095] Calculations of sequence identity are often performed as follows. Sequences are aligned for optimal comparison purposes (e.g., gaps can be introduced in one or both of a first and a second amino acid or nucleic acid sequence for optimal alignment and non-homologous sequences can be disregarded for comparison purposes). The length of a reference sequence aligned for comparison purposes is sometimes 30% or more, 40% or more, 50% or more, often 60% or more, and more often 70% or more, 80% or more, 90% or more, 90% or more, or 100% of the length of the reference sequence. The nucleotides or amino acids at corresponding nucleotide or polypeptide positions, respectively, are then compared among the two sequences. When a position in the first sequence is occupied by the same nucleotide or amino acid as the corresponding position in the second sequence, the nucleotides or amino acids are deemed to be identical at that position. The percent identity between the two sequences is a function of the number of identical positions shared by the sequences,

taking into account the number of gaps, and the length of each gap, introduced for optimal alignment of the two sequences.

[0096] Comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm. Percent identity between two amino acid or nucleotide sequences can be determined using the algorithm of Meyers & Miller, *CABIOS* 4: 11-17 (1989), which has been incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4. Also, percent identity between two amino acid sequences can be determined using the Needleman & Wunsch, *J. Mol. Biol.* 48: 444-453 (1970) algorithm which has been incorporated into the GAP program in the GCG software package (available at the http address www.gcg.com), using either a Blossum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. Percent identity between two nucleotide sequences can be determined using the GAP program in the GCG software package (available at http address www.gcg.com), using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. A set of parameters often used is a Blossum 62 scoring matrix with a gap open penalty of 12, a gap extend penalty of 4, and a frameshift gap penalty of 5.

[0097] Another manner for determining if two nucleic acids are substantially identical is to assess whether a polynucleotide homologous to one nucleic acid will hybridize to the other nucleic acid under stringent conditions. As use herein, the term "stringent conditions" refers to conditions for hybridization and washing. Stringent conditions are known to those skilled in the art and can be found in *Current Protocols in Molecular Biology*, John Wiley & Sons, N.Y., 6.3.1-6.3.6 (1989). Aqueous and non-aqueous methods are described in that reference and either can be used. An example of stringent hybridization conditions is hybridization in 6X sodium chloride/sodium citrate (SSC) at about 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 50°C. Another example of stringent hybridization conditions are hybridization in 6X sodium chloride/sodium citrate (SSC) at about 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 55°C. A further example of stringent hybridization conditions is hybridization in 6X sodium chloride/sodium citrate (SSC) at about 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 60°C. Often, stringent hybridization conditions are hybridization in 6X sodium chloride/sodium citrate (SSC) at about 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 65°C. More often, stringency conditions are 0.5M sodium phosphate, 7% SDS at 65°C, followed by one or more washes at 0.2X SSC, 1% SDS at 65°C.

[0098] An example of a substantially identical nucleotide sequence to a *DLG1*, *KIAA0783*, *DPF3* or *CENPCI* nucleotide sequence is one that has a different nucleotide sequence but still encodes the same polypeptide sequence encoded by the *DLG1*, *KIAA0783*, *DPF3* or *CENPCI* nucleotide sequence. Another example is a nucleotide sequence that encodes a polypeptide having a polypeptide

sequence that is more than 70% or more identical to, sometimes 75% or more, 80% or more, or 85% or more identical to, and often 90% or more and 95% or more identical to a polypeptide sequence encoded by a *DLG1*, *KIAA0783*, *DPF3* or *CENPCI* nucleotide sequence.

[0099] *DLG1*, *KIAA0783*, *DPF3* or *CENPCI* nucleotide sequences and *DLG1*, *KIAA0783*, *DPF3* or *CENPCI* amino acid sequences can be used as “query sequences” to perform a search against public databases to identify other family members or related sequences, for example. Such searches can be performed using the NBLAST and XBLAST programs (version 2.0) of Altschul *et al.*, *J. Mol. Biol.* 215: 403-10 (1990). BLAST nucleotide searches can be performed with the NBLAST program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to nucleotide sequences from SEQ ID NO: 1-8. BLAST polypeptide searches can be performed with the XBLAST program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to polypeptides encoded by a *DLG1*, *KIAA0783*, *DPF3* or *CENPCI* nucleotide sequence. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul *et al.*, *Nucleic Acids Res.* 25(17): 3389-3402 (1997). When utilizing BLAST and Gapped BLAST programs, default parameters of the respective programs (*e.g.*, XBLAST and NBLAST) can be used (*see* the [http address www.ncbi.nlm.nih.gov](http://www.ncbi.nlm.nih.gov)).

[0100] A nucleic acid that is substantially identical to a *DLG1*, *KIAA0783*, *DPF3* or *CENPCI* nucleotide sequence may include polymorphic sites at positions equivalent to those described herein when the sequences are aligned. For example, using the alignment procedures described herein, SNPs in a sequence substantially identical to a sequence in SEQ ID NO: 1-8 can be identified at nucleotide positions that match (*i.e.*, align) with nucleotides at SNP positions in the nucleotide sequence of SEQ ID NO: 1-8. Also, where a polymorphic variation results in an insertion or deletion, insertion or deletion of a nucleotide sequence from a reference sequence can change the relative positions of other polymorphic sites in the nucleotide sequence.

[0101] Substantially identical nucleotide and polypeptide sequences include those that are naturally occurring, such as allelic variants (same locus), splice variants, homologs (different locus), and orthologs (different organism) or can be non-naturally occurring. Non-naturally occurring variants can be generated by mutagenesis techniques, including those applied to polynucleotides, cells, or organisms. The variants can contain nucleotide substitutions, deletions, inversions and insertions. Variation can occur in either or both the coding and non-coding regions. The variations can produce both conservative and non-conservative amino acid substitutions (as compared in the encoded product). Orthologs, homologs, allelic variants, and splice variants can be identified using methods known in the art. These variants normally comprise a nucleotide sequence encoding a polypeptide that is 50% or more, about 55% or more, often about 70-75% or more, more often about 80-85% or more, and typically about 90-95% or more identical to the amino acid sequences of target polypeptides or a fragment thereof. Such nucleic acid molecules readily can be identified as being able to hybridize under stringent conditions to a nucleotide sequence in SEQ ID NO: 1-8 or a

fragment thereof. Nucleic acid molecules corresponding to orthologs, homologs, and allelic variants of a nucleotide sequence in SEQ ID NO: 1-8 can be identified by mapping the sequence to the same chromosome or locus as the nucleotide sequence in SEQ ID NO: 1-8.

[0102] Also, substantially identical nucleotide sequences may include codons that are altered with respect to the naturally occurring sequence for enhancing expression of a target polypeptide in a particular expression system. For example, the nucleic acid can be one in which one or more codons are altered, and often 10% or more or 20% or more of the codons are altered for optimized expression in bacteria (*e.g.*, *E. coli.*), yeast (*e.g.*, *S. cerevisiae*), human (*e.g.*, 293 cells), insect, or rodent (*e.g.*, hamster) cells.

Methods for Identifying Subjects at Risk of Breast Cancer and Breast Cancer Risk in a Subject

[0103] Methods for prognosing and diagnosing breast cancer in subjects are provided herein. These methods include detecting the presence or absence of one or more polymorphic variations associated with breast cancer in a nucleotide sequence set forth in SEQ ID NO: 1-4, or substantially identical sequence thereof, in a sample from a subject, where the presence of a polymorphic variant is indicative of a risk of breast cancer.

[0104] Thus, featured herein is a method for detecting a subject at risk of breast cancer or the risk of breast cancer in a subject, which comprises detecting the presence or absence of a polymorphic variation associated with breast cancer at a polymorphic site in a nucleotide sequence set forth in SEQ ID NO: 1-4 in a nucleic acid sample from a subject, where the nucleotide sequence comprises a polynucleotide sequence selected from the group consisting of: (a) a nucleotide sequence set forth in SEQ ID NO: 1-4; (b) a nucleotide sequence which encodes a polypeptide having an amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-4; (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to an amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-4 or a nucleotide sequence about 90% or more identical to the nucleotide sequence set forth in SEQ ID NO: 1-4; and (d) a fragment of a nucleotide sequence of (a), (b), or (c), often a fragment that includes a polymorphic site associated with breast cancer; whereby the presence of the polymorphic variation is indicative of a risk of breast cancer in the subject. In certain embodiments, determining the presence of a combination of two or more polymorphic variants associated with breast cancer in one or more nucleotide sequences of the sample is determined to identify a subject at risk of breast cancer and/or risk of breast cancer.

[0105] A risk of developing aggressive forms of breast cancer likely to metastasize or invade surrounding tissues (*e.g.*, Stage IIIA, IIIB, and IV breast cancers), and subjects at risk of developing aggressive forms of breast cancer also may be identified by the methods described herein. These methods include collecting phenotype information from subjects having breast cancer, which includes the stage of progression of the breast cancer, and performing a secondary phenotype analysis to detect

the presence or absence of one or more polymorphic variations associated with a particular stage form of breast cancer. Thus, detecting the presence or absence of one or more polymorphic variations in a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleotide sequence associated with a late stage form of breast cancer often is prognostic and/or diagnostic of an aggressive form of the cancer.

[0106] Results from prognostic tests may be combined with other test results to diagnose breast cancer. For example, prognostic results may be gathered, a patient sample may be ordered based on a determined predisposition to breast cancer, the patient sample is analyzed, and the results of the analysis may be utilized to diagnose breast cancer. Also breast cancer diagnostic methods can be developed from studies used to generate prognostic/diagnostic methods in which populations are stratified into subpopulations having different progressions of breast cancer. In another embodiment, prognostic results may be gathered; a patient's risk factors for developing breast cancer analyzed (*e.g.*, age, race, family history, age of first menstrual cycle, age at birth of first child); and a patient sample may be ordered based on a determined predisposition to breast cancer. In an alternative embodiment, the results from predisposition analyses described herein may be combined with other test results indicative of breast cancer, which were previously, concurrently, or subsequently gathered with respect to the predisposition testing. In these embodiments, the combination of the prognostic test results with other test results can be probative of breast cancer, and the combination can be utilized as a breast cancer diagnostic. The results of any test indicative of breast cancer known in the art may be combined with the methods described herein. Examples of such tests are mammography (*e.g.*, a more frequent and/or earlier mammography regimen may be prescribed); breast biopsy and optionally a biopsy from another tissue; breast ultrasound and optionally an ultrasound analysis of another tissue; breast magnetic resonance imaging (MRI) and optionally an MRI analysis of another tissue; electrical impedance (T-scan) analysis of breast and optionally of another tissue; ductal lavage; nuclear medicine analysis (*e.g.*, scintimammography); *BRCA1* and/or *BRCA2* sequence analysis results; and thermal imaging of the breast and optionally of another tissue. Testing may be performed on tissue other than breast to diagnose the occurrence of metastasis (*e.g.*, testing of the lymph node).

[0107] Risk of breast cancer sometimes is expressed as a probability, such as an odds ratio, percentage, or risk factor. The risk is based upon the presence or absence of one or more polymorphic variants described herein, and also may be based in part upon phenotypic traits of the individual being tested. Methods for calculating predispositions based upon patient data are well known (*see, e.g.*, Agresti, *Categorical Data Analysis*, 2nd Ed. 2002. Wiley). Allelotyping and genotyping analyses may be carried out in populations other than those exemplified herein to enhance the predictive power of the prognostic method. These further analyses are executed in view of the exemplified procedures described herein, and may be based upon the same polymorphic variations or additional polymorphic variations. Risk determinations for breast cancer are useful in a variety of applications. In one embodiment, breast cancer risk determinations are used by clinicians to direct appropriate detection, preventative and treatment procedures to subjects who most require these. In another embodiment,

breast cancer risk determinations are used by health insurers for preparing actuarial tables and for calculating insurance premiums.

[0108] The nucleic acid sample typically is isolated from a biological sample obtained from a subject. For example, nucleic acid can be isolated from blood, saliva, sputum, urine, cell scrapings, and biopsy tissue. The nucleic acid sample can be isolated from a biological sample using standard techniques, such as the technique described in Example 2. As used herein, the term “subject” refers primarily to humans but also refers to other mammals such as dogs, cats, and ungulates (*e.g.*, cattle, sheep, and swine). Subjects also include avians (*e.g.*, chickens and turkeys), reptiles, and fish (*e.g.*, salmon), as embodiments described herein can be adapted to nucleic acid samples isolated from any of these organisms. The nucleic acid sample may be isolated from the subject and then directly utilized in a method for determining the presence of a polymorphic variant, or alternatively, the sample may be isolated and then stored (*e.g.*, frozen) for a period of time before being subjected to analysis.

[0109] The presence or absence of a polymorphic variant is determined using one or both chromosomal complements represented in the nucleic acid sample. Determining the presence or absence of a polymorphic variant in both chromosomal complements represented in a nucleic acid sample from a subject having a copy of each chromosome is useful for determining the zygosity of an individual for the polymorphic variant (*i.e.*, whether the individual is homozygous or heterozygous for the polymorphic variant). Any oligonucleotide-based diagnostic may be utilized to determine whether a sample includes the presence or absence of a polymorphic variant in a sample. For example, primer extension methods, ligase sequence determination methods (*e.g.*, U.S. Pat. Nos. 5,679,524 and 5,952,174, and WO 01/27326), mismatch sequence determination methods (*e.g.*, U.S. Pat. Nos. 5,851,770; 5,958,692; 6,110,684; and 6,183,958), microarray sequence determination methods, restriction fragment length polymorphism (RFLP), single strand conformation polymorphism detection (SSCP) (*e.g.*, U.S. Pat. Nos. 5,891,625 and 6,013,499), PCR-based assays (*e.g.*, TAQMAN[®] PCR System (Applied Biosystems)), and nucleotide sequencing methods may be used.

[0110] Oligonucleotide extension methods typically involve providing a pair of oligonucleotide primers in a polymerase chain reaction (PCR) or in other nucleic acid amplification methods for the purpose of amplifying a region from the nucleic acid sample that comprises the polymorphic variation. One oligonucleotide primer is complementary to a region 3' of the polymorphism and the other is complementary to a region 5' of the polymorphism. A PCR primer pair may be used in methods disclosed in U.S. Pat. Nos. 4,683,195; 4,683,202, 4,965,188; 5,656,493; 5,998,143; 6,140,054; WO 01/27327; and WO 01/27329 for example. PCR primer pairs may also be used in any commercially available machines that perform PCR, such as any of the GENEAMP[®] Systems available from Applied Biosystems. Also, those of ordinary skill in the art will be able to design oligonucleotide primers based upon a nucleotide sequence set forth in SEQ ID NO: 1-4 without undue experimentation using knowledge readily available in the art.

[0111] Also provided is an extension oligonucleotide that hybridizes to the amplified fragment adjacent to the polymorphic variation. As used herein, the term “adjacent” refers to the 3’ end of the extension oligonucleotide being often 1 nucleotide from the 5’ end of the polymorphic site, and sometimes 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotides from the 5’ end of the polymorphic site, in the nucleic acid when the extension oligonucleotide is hybridized to the nucleic acid. The extension oligonucleotide then is extended by one or more nucleotides, and the number and/or type of nucleotides that are added to the extension oligonucleotide determine whether the polymorphic variant is present. Oligonucleotide extension methods are disclosed, for example, in U.S. Pat. Nos. 4,656,127; 4,851,331; 5,679,524; 5,834,189; 5,876,934; 5,908,755; 5,912,118; 5,976,802; 5,981,186; 6,004,744; 6,013,431; 6,017,702; 6,046,005; 6,087,095; 6,210,891; and WO 01/20039. Oligonucleotide extension methods using mass spectrometry are described, for example, in U.S. Pat. Nos. 5,547,835; 5,605,798; 5,691,141; 5,849,542; 5,869,242; 5,928,906; 6,043,031; and 6,194,144, and a method often utilized is described herein in Example 2. Multiple extension oligonucleotides may be utilized in one reaction, which is referred to herein as “multiplexing.”

[0112] A microarray can be utilized for determining whether a polymorphic variant is present or absent in a nucleic acid sample. A microarray may include any oligonucleotides described herein, and methods for making and using oligonucleotide microarrays suitable for diagnostic use are disclosed in U.S. Pat. Nos. 5,492,806; 5,525,464; 5,589,330; 5,695,940; 5,849,483; 6,018,041; 6,045,996; 6,136,541; 6,142,681; 6,156,501; 6,197,506; 6,223,127; 6,225,625; 6,229,911; 6,239,273; WO 00/52625; WO 01/25485; and WO 01/29259. The microarray typically comprises a solid support and the oligonucleotides may be linked to this solid support by covalent bonds or by non-covalent interactions. The oligonucleotides may also be linked to the solid support directly or by a spacer molecule. A microarray may comprise one or more oligonucleotides complementary to a polymorphic site set forth in SEQ ID NO: 1-4 or below.

[0113] A kit also may be utilized for determining whether a polymorphic variant is present or absent in a nucleic acid sample. A kit often comprises one or more pairs of oligonucleotide primers useful for amplifying a fragment of a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleotide sequence or a substantially identical sequence thereof, where the fragment includes a polymorphic site. The kit sometimes comprises a polymerizing agent, for example, a thermostable nucleic acid polymerase such as one disclosed in U.S. Pat. Nos. 4,889,818 or 6,077,664. Also, the kit often comprises an elongation oligonucleotide that hybridizes to a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleotide sequence in a nucleic acid sample adjacent to the polymorphic site. Where the kit includes an elongation oligonucleotide, it also often comprises chain elongating nucleotides, such as dATP, dTTP, dGTP, dCTP, and dITP, including analogs of dATP, dTTP, dGTP, dCTP and dITP, provided that such analogs are substrates for a thermostable nucleic acid polymerase and can be incorporated into a nucleic acid chain elongated from the extension oligonucleotide. Along with chain elongating nucleotides would be one or more chain terminating nucleotides such as ddATP, ddTTP, ddGTP,

ddCTP, and the like. In an embodiment, the kit comprises one or more oligonucleotide primer pairs, a polymerizing agent, chain elongating nucleotides, at least one elongation oligonucleotide, and one or more chain terminating nucleotides. Kits optionally include buffers, vials, microtiter plates, and instructions for use.

[0114] An individual identified as being at risk of breast cancer may be heterozygous or homozygous with respect to the allele associated with a higher risk of breast cancer. A subject homozygous for an allele associated with an increased risk of breast cancer is at a comparatively high risk of breast cancer, a subject heterozygous for an allele associated with an increased risk of breast cancer is at a comparatively intermediate risk of breast cancer, and a subject homozygous for an allele associated with a decreased risk of breast cancer is at a comparatively low risk of breast cancer. A genotype may be assessed for a complementary strand, such that the complementary nucleotide at a particular position is detected.

[0115] Also featured are methods for determining risk of breast cancer and/or identifying a subject at risk of breast cancer by contacting a polypeptide or protein encoded by a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleotide sequence from a subject with an antibody that specifically binds to an epitope associated with increased risk of breast cancer in the polypeptide. In certain embodiments, the antibody specifically binds to an epitope that comprises a glutamine at amino acid position 278 in SEQ ID NO: 9 or a glycine at amino acid position 389 in SEQ ID NO: 12.

Applications of Prognostic and Diagnostic Results to Pharmacogenomic Methods

[0116] Pharmacogenomics is a discipline that involves tailoring a treatment for a subject according to the subject's genotype. For example, based upon the outcome of a prognostic test described herein, a clinician or physician may target pertinent information and preventative or therapeutic treatments to a subject who would be benefited by the information or treatment and avoid directing such information and treatments to a subject who would not be benefited (*e.g.*, the treatment has no therapeutic effect and/or the subject experiences adverse side effects). As therapeutic approaches for breast cancer continue to evolve and improve, the goal of treatments for breast cancer related disorders is to intervene even before clinical signs (*e.g.*, identification of lump in the breast) first manifest. Thus, genetic markers associated with susceptibility to breast cancer prove useful for early diagnosis, prevention and treatment of breast cancer.

[0117] The following is an example of a pharmacogenomic embodiment. A particular treatment regimen can exert a differential effect depending upon the subject's genotype. Where a candidate therapeutic exhibits a significant interaction with a major allele and a comparatively weak interaction with a minor allele (*e.g.*, an order of magnitude or greater difference in the interaction), such a therapeutic typically would not be administered to a subject genotyped as being homozygous for the minor allele, and sometimes not administered to a subject genotyped as being heterozygous for the minor allele. In another example, where a candidate therapeutic is not significantly toxic when

administered to subjects who are homozygous for a major allele but is comparatively toxic when administered to subjects heterozygous or homozygous for a minor allele, the candidate therapeutic is not typically administered to subjects who are genotyped as being heterozygous or homozygous with respect to the minor allele.

[0118] The methods described herein are applicable to pharmacogenomic methods for detecting, preventing, alleviating and/or treating breast cancer. For example, a nucleic acid sample from an individual may be subjected to a genetic test described herein. Where one or more polymorphic variations associated with increased risk of breast cancer are identified in a subject, information for detecting, preventing or treating breast cancer and/or one or more breast cancer detection, prevention and/or treatment regimens then may be directed to and/or prescribed to that subject.

[0119] In certain embodiments, a detection, prevenative and/or treatment regimen is specifically prescribed and/or administered to individuals who will most benefit from it based upon their risk of developing breast cancer assessed by the methods described herein. Thus, provided are methods for identifying a subject at risk of breast cancer and then prescribing a detection, therapeutic or preventative regimen to individuals identified as being at risk of breast cancer. Thus, certain embodiments are directed to methods for treating breast cancer in a subject, reducing risk of breast cancer in a subject, or early detection of breast cancer in a subject, which comprise: detecting the presence or absence of a polymorphic variant associated with breast cancer in a nucleotide sequence in a nucleic acid sample from a subject, where the nucleotide sequence comprises a polynucleotide sequence selected from the group consisting of: (a) a nucleotide sequence set forth in SEQ ID NO: 1-4; (b) a nucleotide sequence which encodes a polypeptide having an amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-4; (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to an amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-4 or a nucleotide sequence about 90% or more identical to the nucleotide sequence set forth in SEQ ID NO: 1-4; and (d) a fragment of a nucleotide sequence of (a), (b), or (c), sometimes comprising a polymorphic site associated with breast cancer; and prescribing or administering a breast cancer treatment regimen, preventative regimen and/or detection regimen to a subject from whom the sample originated where the presence of one or more polymorphic variations associated with breast cancer are detected in the nucleotide sequence. In these methods, genetic results may be utilized in combination with other test results to diagnose breast cancer as described above. Other test results include but are not limited to mammography results, imaging results, biopsy results and results from *BRCA1* or *BRAC2* test results, as described above.

[0120] Detection regimens include one or more mammography procedures, a regular mammography regimen (*e.g.*, once a year, or once every six, four, three or two months); an early mammography regimen (*e.g.*, mammography tests are performed beginning at age 25, 30, or 35); one or more biopsy procedures (*e.g.*, a regular biopsy regimen beginning at age 40); breast biopsy and biopsy from other tissue; breast ultrasound and optionally ultrasound analysis of another tissue; breast

magnetic resonance imaging (MRI) and optionally MRI analysis of another tissue; electrical impedance (T-scan) analysis of breast and optionally another tissue; ductal lavage; nuclear medicine analysis (*e.g.*, scintimammography); *BRCA1* and/or *BRCA2* sequence analysis results; and/or thermal imaging of the breast and optionally another tissue.

[0121] Treatments sometimes are preventative (*e.g.*, is prescribed or administered to reduce the probability that a breast cancer associated condition arises or progresses), sometimes are therapeutic, and sometimes delay, alleviate or halt the progression of breast cancer. Any known preventative or therapeutic treatment for alleviating or preventing the occurrence of breast cancer is prescribed and/or administered. For example, certain preventative treatments often are prescribed to subjects having a predisposition to breast cancer and where the subject is not diagnosed with breast cancer or is diagnosed as having symptoms indicative of early stage breast cancer (*e.g.*, stage I). For subjects not diagnosed as having breast cancer, any preventative treatments known in the art can be prescribed and administered, which include selective hormone receptor modulators (*e.g.*, selective estrogen receptor modulators (SERMs) such as tamoxifen, reloxifene, and toremifene); compositions that prevent production of hormones (*e.g.*, aromatase inhibitors that prevent the production of estrogen in the adrenal gland, such as exemestane, letrozole, anastrozol, goserelin, and megestrol); other hormonal treatments (*e.g.*, goserelin acetate and fulvestrant); biologic response modifiers such as antibodies (*e.g.*, trastuzumab (herceptin/HER2)); surgery (*e.g.*, lumpectomy and mastectomy); drugs that delay or halt metastasis (*e.g.*, pamidronate disodium); and alternative/complementary medicine (*e.g.*, acupuncture, acupressure, moxibustion, qi gong, reiki, ayurveda, vitamins, minerals, and herbs (*e.g.*, astragalus root, burdock root, garlic, green tea, and licorice root)).

[0122] The use of breast cancer treatments are well known in the art, and include surgery, chemotherapy and/or radiation therapy. Any of the treatments may be used in combination to treat or prevent breast cancer (*e.g.*, surgery followed by radiation therapy or chemotherapy). Examples of chemotherapy combinations used to treat breast cancer include: cyclophosphamide (Cytosan), methotrexate (Amethopterin, Mexate, Folex), and fluorouracil (Fluorouracil, 5-Fu, Adrucil), which is referred to as CMF; cyclophosphamide, doxorubicin (Adriamycin), and fluorouracil, which is referred to as CAF; and doxorubicin (Adriamycin) and cyclophosphamide, which is referred to as AC.

[0123] As breast cancer preventative and treatment information can be specifically targeted to subjects in need thereof (*e.g.*, those at risk of developing breast cancer or those that have early signs of breast cancer), provided herein is a method for preventing or reducing the risk of developing breast cancer in a subject, which comprises: (a) detecting the presence or absence of a polymorphic variation associated with breast cancer at a polymorphic site in a nucleotide sequence in a nucleic acid sample from a subject; (b) identifying a subject with a predisposition to breast cancer, whereby the presence of the polymorphic variation is indicative of a predisposition to breast cancer in the subject; and (c) if such a predisposition is identified, providing the subject with information about methods or products to prevent or reduce breast cancer or to delay the onset of breast cancer. Also provided is a method of

targeting information or advertising to a subpopulation of a human population based on the subpopulation being genetically predisposed to a disease or condition, which comprises: (a) detecting the presence or absence of a polymorphic variation associated with breast cancer at a polymorphic site in a nucleotide sequence in a nucleic acid sample from a subject; (b) identifying the subpopulation of subjects in which the polymorphic variation is associated with breast cancer; and (c) providing information only to the subpopulation of subjects about a particular product which may be obtained and consumed or applied by the subject to help prevent or delay onset of the disease or condition.

[0124] Pharmacogenomics methods also may be used to analyze and predict a response to a breast cancer treatment or a drug. For example, if pharmacogenomics analysis indicates a likelihood that an individual will respond positively to a breast cancer treatment with a particular drug, the drug may be administered to the individual. Conversely, if the analysis indicates that an individual is likely to respond negatively to treatment with a particular drug, an alternative course of treatment may be prescribed. A negative response may be defined as either the absence of an efficacious response or the presence of toxic side effects. The response to a therapeutic treatment can be predicted in a background study in which subjects in any of the following populations are genotyped: a population that responds favorably to a treatment regimen, a population that does not respond significantly to a treatment regimen, and a population that responds adversely to a treatment regimen (*e.g.*, exhibits one or more side effects). These populations are provided as examples and other populations and subpopulations may be analyzed. Based upon the results of these analyses, a subject is genotyped to predict whether he or she will respond favorably to a treatment regimen, not respond significantly to a treatment regimen, or respond adversely to a treatment regimen.

[0125] The methods described herein also are applicable to clinical drug trials. One or more polymorphic variants indicative of response to an agent for treating breast cancer or to side effects to an agent for treating breast cancer may be identified using the methods described herein. Thereafter, potential participants in clinical trials of such an agent may be screened to identify those individuals most likely to respond favorably to the drug and exclude those likely to experience side effects. In that way, the effectiveness of drug treatment may be measured in individuals who respond positively to the drug, without lowering the measurement as a result of the inclusion of individuals who are unlikely to respond positively in the study and without risking undesirable safety problems. In certain embodiments, the agent for treating breast cancer described herein targets *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* or a target in the *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* pathway.

[0126] Thus, another embodiment is a method of selecting an individual for inclusion in a clinical trial of a treatment or drug comprising the steps of: (a) obtaining a nucleic acid sample from an individual; (b) determining the identity of a polymorphic variation which is associated with a positive response to the treatment or the drug, or at least one polymorphic variation which is associated with a negative response to the treatment or the drug in the nucleic acid sample, and (c) including the individual in the clinical trial if the nucleic acid sample contains said polymorphic

variation associated with a positive response to the treatment or the drug or if the nucleic acid sample lacks said polymorphic variation associated with a negative response to the treatment or the drug. In addition, the methods for selecting an individual for inclusion in a clinical trial of a treatment or drug encompass methods with any further limitation described in this disclosure, or those following, specified alone or in any combination. The polymorphic variation may be in a sequence selected individually or in any combination from the group consisting of (i) a polynucleotide sequence set forth in SEQ ID NO: 1-4; (ii) a polynucleotide sequence that is 90% or more identical to a nucleotide sequence set forth in SEQ ID NO: 1-4; (iii) a polynucleotide sequence that encodes a polypeptide having an amino acid sequence identical to or 90% or more identical to an amino acid sequence encoded by a nucleotide sequence set forth in SEQ ID NO: 1-4; and (iv) a fragment of a polynucleotide sequence of (i), (ii), or (iii) comprising the polymorphic site. The including step (c) optionally comprises administering the drug or the treatment to the individual if the nucleic acid sample contains the polymorphic variation associated with a positive response to the treatment or the drug and the nucleic acid sample lacks said biallelic marker associated with a negative response to the treatment or the drug.

[0127] Also provided herein is a method of partnering between a diagnostic/prognostic testing provider and a provider of a consumable product, which comprises: (a) the diagnostic/prognostic testing provider detects the presence or absence of a polymorphic variation associated with breast cancer at a polymorphic site in a nucleotide sequence in a nucleic acid sample from a subject; (b) the diagnostic/prognostic testing provider identifies the subpopulation of subjects in which the polymorphic variation is associated with breast cancer; (c) the diagnostic/prognostic testing provider forwards information to the subpopulation of subjects about a particular product which may be obtained and consumed or applied by the subject to help prevent or delay onset of the disease or condition; and (d) the provider of a consumable product forwards to the diagnostic test provider a fee every time the diagnostic/prognostic test provider forwards information to the subject as set forth in step (c) above.

Compositions Comprising Breast Cancer-Directed Molecules

[0128] Featured herein is a composition comprising a breast cancer cell and one or more molecules specifically directed and targeted to a nucleic acid comprising a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleotide sequence or a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide. Such directed molecules include, but are not limited to, a compound that binds to a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acid or a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide; a RNAi or siRNA molecule having a strand complementary to a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleotide sequence; an antisense nucleic acid complementary to an RNA encoded by a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* DNA sequence; a ribozyme that hybridizes to a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleotide sequence; a nucleic acid aptamer that specifically binds a *DLG1*,

KIAA0783, *DPF3* or *CENPC1* polypeptide; and an antibody that specifically binds to a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide or binds to a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acid. In certain embodiments, the antibody specifically binds to an epitope that comprises a glutamine at amino acid position 278 in SEQ ID NO: 9 or a glycine at amino acid position 389 in SEQ ID NO: 12. In specific embodiments, the breast cancer directed molecule interacts with a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acid or polypeptide variant associated with breast cancer. In other embodiments, the breast cancer directed molecule interacts with a polypeptide involved in the *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* signal pathway, or a nucleic acid encoding such a polypeptide. Polypeptides involved in the *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* signal pathway are discussed herein.

[0129] Compositions sometimes include an adjuvant known to stimulate an immune response, and in certain embodiments, an adjuvant that stimulates a T-cell lymphocyte response. Adjuvants are known, including but not limited to an aluminum adjuvant (*e.g.*, aluminum hydroxide); a cytokine adjuvant or adjuvant that stimulates a cytokine response (*e.g.*, interleukin (IL)-12 and/or γ -interferon cytokines); a Freund-type mineral oil adjuvant emulsion (*e.g.*, Freund's complete or incomplete adjuvant); a synthetic lipid compound; a copolymer adjuvant (*e.g.*, TitreMax); a saponin; Quil A; a liposome; an oil-in-water emulsion (*e.g.*, an emulsion stabilized by Tween 80 and pluronic polyoxyethylene/polyoxypropylene block copolymer (Syntex Adjuvant Formulation); TitreMax; detoxified endotoxin (MPL) and mycobacterial cell wall components (TDW, CWS) in 2% squalene (Ribi Adjuvant System)); a muramyl dipeptide; an immune-stimulating complex (ISCOM, *e.g.*, an Ag-modified saponin/cholesterol micelle that forms stable cage-like structure); an aqueous phase adjuvant that does not have a depot effect (*e.g.*, Gerbu adjuvant); a carbohydrate polymer (*e.g.*, AdjuPrime); L-tyrosine; a manide-oleate compound (*e.g.*, Montanide); an ethylene-vinyl acetate copolymer (*e.g.*, Elvax 40W1,2); or lipid A, for example. Such compositions are useful for generating an immune response against a breast cancer directed molecule (*e.g.*, an HLA-binding subsequence within a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-4). In such methods, a peptide having an amino acid subsequence of a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-4 is delivered to a subject, where the subsequence binds to an HLA molecule and induces a CTL lymphocyte response. The peptide sometimes is delivered to the subject as an isolated peptide or as a minigene in a plasmid that encodes the peptide. Methods for identifying HLA-binding subsequences in such polypeptides are known (*see e.g.*, publication WO02/20616 and PCT application US98/01373 for methods of identifying such sequences).

[0130] The breast cancer cell may be in a group of breast cancer cells and/or other types of cells cultured *in vitro* or in a tissue having breast cancer cells (*e.g.*, a melanocytic lesion) maintained *in vitro* or present in an animal *in vivo* (*e.g.*, a rat, mouse, ape or human). In certain embodiments, a composition comprises a component from a breast cancer cell or from a subject having a breast cancer cell instead of the breast cancer cell or in addition to the breast cancer cell, where the component

sometimes is a nucleic acid molecule (*e.g.*, genomic DNA), a protein mixture or isolated protein, for example. The aforementioned compositions have utility in diagnostic, prognostic and pharmacogenomic methods described previously and in breast cancer therapeutics described hereafter. Certain breast cancer molecules are described in greater detail below.

Compounds

[0131] Compounds can be obtained using any of the numerous approaches in combinatorial library methods known in the art, including: biological libraries; peptoid libraries (libraries of molecules having the functionalities of peptides, but with a novel, non-peptide backbone which are resistant to enzymatic degradation but which nevertheless remain bioactive (see, *e.g.*, Zuckermann *et al.*, J. Med. Chem. 37: 2678-85 (1994)); spatially addressable parallel solid phase or solution phase libraries; synthetic library methods requiring deconvolution; "one-bead one-compound" library methods; and synthetic library methods using affinity chromatography selection. Biological library and peptoid library approaches are typically limited to peptide libraries, while the other approaches are applicable to peptide, non-peptide oligomer or small molecule libraries of compounds (Lam, Anticancer Drug Des. 12: 145, (1997)). Examples of methods for synthesizing molecular libraries are described, for example, in DeWitt *et al.*, Proc. Natl. Acad. Sci. U.S.A. 90: 6909 (1993); Erb *et al.*, Proc. Natl. Acad. Sci. USA 91: 11422 (1994); Zuckermann *et al.*, J. Med. Chem. 37: 2678 (1994); Cho *et al.*, Science 261: 1303 (1993); Carrell *et al.*, Angew. Chem. Int. Ed. Engl. 33: 2059 (1994); Carell *et al.*, Angew. Chem. Int. Ed. Engl. 33: 2061 (1994); and in Gallop *et al.*, J. Med. Chem. 37: 1233 (1994).

[0132] Libraries of compounds may be presented in solution (*e.g.*, Houghten, Biotechniques 13: 412-421 (1992)), or on beads (Lam, Nature 354: 82-84 (1991)), chips (Fodor, Nature 364: 555-556 (1993)), bacteria or spores (Ladner, United States Patent No. 5,223,409), plasmids (Cull *et al.*, Proc. Natl. Acad. Sci. USA 89: 1865-1869 (1992)) or on phage (Scott and Smith, Science 249: 386-390 (1990); Devlin, Science 249: 404-406 (1990); Cwirla *et al.*, Proc. Natl. Acad. Sci. 87: 6378-6382 (1990); Felici, J. Mol. Biol. 222: 301-310 (1991); Ladner *supra.*).

[0133] A compound sometimes alters expression and sometimes alters activity of a *DLG1*, *KIAA0783*, *DPF3* or *CENPCI* polypeptide and may be a small molecule. Small molecules include, but are not limited to, peptides, peptidomimetics (*e.g.*, peptoids), amino acids, amino acid analogs, polynucleotides, polynucleotide analogs, nucleotides, nucleotide analogs, organic or inorganic compounds (*i.e.*, including heteroorganic and organometallic compounds) having a molecular weight less than about 10,000 grams per mole, organic or inorganic compounds having a molecular weight less than about 5,000 grams per mole, organic or inorganic compounds having a molecular weight less than about 1,000 grams per mole, organic or inorganic compounds having a molecular weight less than about 500 grams per mole, and salts, esters, and other pharmaceutically acceptable forms of such compounds.

Antisense Nucleic Acid Molecules, Ribozymes, RNAi, siRNA and Modified Nucleic Acid Molecules

[0134] An “antisense” nucleic acid refers to a nucleotide sequence complementary to a “sense” nucleic acid encoding a polypeptide, *e.g.*, complementary to the coding strand of a double-stranded cDNA molecule or complementary to an mRNA sequence. The antisense nucleic acid can be complementary to an entire coding strand in SEQ ID NO: 1-8, or to a portion thereof or a substantially identical sequence thereof. In another embodiment, the antisense nucleic acid molecule is antisense to a “noncoding region” of the coding strand of a nucleotide sequence in SEQ ID NO: 1-8 (*e.g.*, 5’ and 3’ untranslated regions).

[0135] An antisense nucleic acid can be designed such that it is complementary to the entire coding region of an mRNA encoded by a nucleotide sequence in SEQ ID NO: 1-4 (*e.g.*, SEQ ID NO: 6-11), and often the antisense nucleic acid is an oligonucleotide antisense to only a portion of a coding or noncoding region of the mRNA. For example, the antisense oligonucleotide can be complementary to the region surrounding the translation start site of the mRNA, *e.g.*, between the -10 and +10 regions of the target gene nucleotide sequence of interest. An antisense oligonucleotide can be, for example, about 7, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, or more nucleotides in length. The antisense nucleic acids, which include the ribozymes described hereafter, can be designed to target a nucleotide sequence in SEQ ID NO: 1-8, often a variant associated with breast cancer, or a substantially identical sequence thereof. Among the variants, minor alleles and major alleles can be targeted, and those associated with a higher risk of breast cancer are often designed, tested, and administered to subjects.

[0136] An antisense nucleic acid can be constructed using chemical synthesis and enzymatic ligation reactions using standard procedures. For example, an antisense nucleic acid (*e.g.*, an antisense oligonucleotide) can be chemically synthesized using naturally occurring nucleotides or variously modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids, *e.g.*, phosphorothioate derivatives and acridine substituted nucleotides can be used. Antisense nucleic acid also can be produced biologically using an expression vector into which a nucleic acid has been subcloned in an antisense orientation (*i.e.*, RNA transcribed from the inserted nucleic acid will be of an antisense orientation to a target nucleic acid of interest, described further in the following subsection).

[0137] When utilized as therapeutics, antisense nucleic acids typically are administered to a subject (*e.g.*, by direct injection at a tissue site) or generated *in situ* such that they hybridize with or bind to cellular mRNA and/or genomic DNA encoding a polypeptide and thereby inhibit expression of the polypeptide, for example, by inhibiting transcription and/or translation. Alternatively, antisense nucleic acid molecules can be modified to target selected cells and then are administered systemically. For systemic administration, antisense molecules can be modified such that they specifically bind to

receptors or antigens expressed on a selected cell surface, for example, by linking antisense nucleic acid molecules to peptides or antibodies which bind to cell surface receptors or antigens. Antisense nucleic acid molecules can also be delivered to cells using the vectors described herein. Sufficient intracellular concentrations of antisense molecules are achieved by incorporating a strong promoter, such as a pol II or pol III promoter, in the vector construct.

[0138] Antisense nucleic acid molecules sometimes are α -anomeric nucleic acid molecules. An α -anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual β -units, the strands run parallel to each other (Gaultier *et al.*, Nucleic Acids Res. 15: 6625-6641 (1987)). Antisense nucleic acid molecules can also comprise a 2'-O-methylribonucleotide (Inoue *et al.*, Nucleic Acids Res. 15: 6131-6148 (1987)) or a chimeric RNA-DNA analogue (Inoue *et al.*, FEBS Lett. 215: 327-330 (1987)). Antisense nucleic acids sometimes are composed of DNA or PNA or any other nucleic acid derivatives described previously.

[0139] In another embodiment, an antisense nucleic acid is a ribozyme. A ribozyme having specificity for a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleotide sequence can include one or more sequences complementary to such a nucleotide sequence, and a sequence having a known catalytic region responsible for mRNA cleavage (see *e.g.*, U.S. Pat. No. 5,093,246 or Haselhoff and Gerlach, Nature 334: 585-591 (1988)). For example, a derivative of a Tetrahymena L-19 IVS RNA is sometimes utilized in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved in a mRNA (see *e.g.*, Cech *et al.* U.S. Patent No. 4,987,071; and Cech *et al.* U.S. Patent No. 5,116,742). Also, target mRNA sequences can be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules (see *e.g.*, Bartel & Szostak, Science 261: 1411-1418 (1993)).

[0140] Breast cancer directed molecules include in certain embodiments nucleic acids that can form triple helix structures with a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleotide sequence or a substantially identical sequence thereof, especially one that includes a regulatory region that controls expression of a polypeptide. Gene expression can be inhibited by targeting nucleotide sequences complementary to the regulatory region of a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleotide sequence or a substantially identical sequence (*e.g.*, promoter and/or enhancers) to form triple helical structures that prevent transcription of a gene in target cells (see *e.g.*, Helene, Anticancer Drug Des. 6(6): 569-84 (1991); Helene *et al.*, Ann. N.Y. Acad. Sci. 660: 27-36 (1992); and Maher, Bioassays 14(12): 807-15 (1992). Potential sequences that can be targeted for triple helix formation can be increased by creating a so-called "switchback" nucleic acid molecule. Switchback molecules are synthesized in an alternating 5'-3', 3'-5' manner, such that they base pair with first one strand of a duplex and then the other, eliminating the necessity for a sizeable stretch of either purines or pyrimidines to be present on one strand of a duplex.

[0141] Breast cancer directed molecules include RNAi and siRNA nucleic acids. Gene expression may be inhibited by the introduction of double-stranded RNA (dsRNA), which induces

potent and specific gene silencing, a phenomenon called RNA interference or RNAi. See, *e.g.*, Fire *et al.*, US Patent Number 6,506,559; Tuschl *et al.* PCT International Publication No. WO 01/75164; Kay *et al.* PCT International Publication No. WO 03/010180A1; or Bosher JM, Labouesse, Nat Cell Biol 2000 Feb;2(2):E31-6. This process has been improved by decreasing the size of the double-stranded RNA to 20-24 base pairs (to create small-interfering RNAs or siRNAs) that “switched off” genes in mammalian cells without initiating an acute phase response, i.e., a host defense mechanism that often results in cell death (see, *e.g.*, Caplen *et al.* Proc Natl Acad Sci U S A. 2001 Aug 14;98(17):9742-7 and Elbashir *et al.* Methods 2002 Feb;26(2):199-213). There is increasing evidence of post-transcriptional gene silencing by RNA interference (RNAi) for inhibiting targeted expression in mammalian cells at the mRNA level, in human cells. There is additional evidence of effective methods for inhibiting the proliferation and migration of tumor cells in human patients, and for inhibiting metastatic cancer development (see, *e.g.*, U.S. Patent Application No. US2001000993183; Caplen *et al.* Proc Natl Acad Sci U S A; and Abderrahmani *et al.* Mol Cell Biol 2001 Nov21(21):7256-67).

[0142] An “siRNA” or “RNAi” refers to a nucleic acid that forms a double stranded RNA and has the ability to reduce or inhibit expression of a gene or target gene when the siRNA is delivered to or expressed in the same cell as the gene or target gene. “siRNA” refers to short double-stranded RNA formed by the complementary strands. Complementary portions of the siRNA that hybridize to form the double stranded molecule often have substantial or complete identity to the target molecule sequence. In one embodiment, an siRNA refers to a nucleic acid that has substantial or complete identity to a target gene and forms a double stranded siRNA.

[0143] When designing the siRNA molecules, the targeted region often is selected from a given DNA sequence beginning 50 to 100 nucleotides downstream of the start codon. See, *e.g.*, Elbashir *et al.*, Methods 26:199-213 (2002). Initially, 5' or 3' UTRs and regions nearby the start codon were avoided assuming that UTR-binding proteins and/or translation initiation complexes may interfere with binding of the siRNP or RISC endonuclease complex. Sometimes regions of the target 23 nucleotides in length conforming to the sequence motif AA(N19)TT (N, an nucleotide), and regions with approximately 30% to 70% G/C-content (often about 50% G/C-content) often are selected. If no suitable sequences are found, the search often is extended using the motif NA(N21). The sequence of the sense siRNA sometimes corresponds to (N19) TT or N21 (position 3 to 23 of the 23-nt motif), respectively. In the latter case, the 3' end of the sense siRNA often is converted to TT. The rationale for this sequence conversion is to generate a symmetric duplex with respect to the sequence composition of the sense and antisense 3' overhangs. The antisense siRNA is synthesized as the complement to position 1 to 21 of the 23-nt motif. Because position 1 of the 23-nt motif is not recognized sequence-specifically by the antisense siRNA, the 3'-most nucleotide residue of the antisense siRNA can be chosen deliberately. However, the penultimate nucleotide of the antisense siRNA (complementary to position 2 of the 23-nt motif) often is complementary to the targeted

sequence. For simplifying chemical synthesis, TT often is utilized. siRNAs corresponding to the target motif NAR(N17)YNN, where R is purine (A,G) and Y is pyrimidine (C,U), often are selected. Respective 21 nucleotide sense and antisense siRNAs often begin with a purine nucleotide and can also be expressed from pol III expression vectors without a change in targeting site. Expression of RNAs from pol III promoters often is efficient when the first transcribed nucleotide is a purine.

[0144] The sequence of the siRNA can correspond to the full length target gene, or a subsequence thereof. Often, the siRNA is about 15 to about 50 nucleotides in length (*e.g.*, each complementary sequence of the double stranded siRNA is 15-50 nucleotides in length, and the double stranded siRNA is about 15-50 base pairs in length, sometimes about 20-30 nucleotides in length or about 20-25 nucleotides in length, *e.g.*, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 nucleotides in length. The siRNA sometimes is about 21 nucleotides in length. Methods of using siRNA are well known in the art, and specific siRNA molecules may be purchased from a number of companies including Dharmacon Research, Inc.

[0145] Antisense, ribozyme, RNAi and siRNA nucleic acids can be altered to form modified nucleic acid molecules. The nucleic acids can be altered at base moieties, sugar moieties or phosphate backbone moieties to improve stability, hybridization, or solubility of the molecule. For example, the deoxyribose phosphate backbone of nucleic acid molecules can be modified to generate peptide nucleic acids (see Hyrup *et al.*, Bioorganic & Medicinal Chemistry 4 (1): 5-23 (1996)). As used herein, the terms “peptide nucleic acid” or “PNA” refers to a nucleic acid mimic such as a DNA mimic, in which the deoxyribose phosphate backbone is replaced by a pseudopeptide backbone and only the four natural nucleobases are retained. The neutral backbone of a PNA can allow for specific hybridization to DNA and RNA under conditions of low ionic strength. Synthesis of PNA oligomers can be performed using standard solid phase peptide synthesis protocols as described, for example, in Hyrup *et al.*, (1996) *supra* and Perry-O’Keefe *et al.*, Proc. Natl. Acad. Sci. 93: 14670-675 (1996).

[0146] PNA nucleic acids can be used in prognostic, diagnostic, and therapeutic applications. For example, PNAs can be used as antisense or antigene agents for sequence-specific modulation of gene expression by, for example, inducing transcription or translation arrest or inhibiting replication. PNA nucleic acid molecules can also be used in the analysis of single base pair mutations in a gene, (*e.g.*, by PNA-directed PCR clamping); as “artificial restriction enzymes” when used in combination with other enzymes, (*e.g.*, S1 nucleases (Hyrup (1996) *supra*)); or as probes or primers for DNA sequencing or hybridization (Hyrup *et al.*, (1996) *supra*; Perry-O’Keefe *supra*).

[0147] In other embodiments, oligonucleotides may include other appended groups such as peptides (*e.g.*, for targeting host cell receptors *in vivo*), or agents facilitating transport across cell membranes (see *e.g.*, Letsinger *et al.*, Proc. Natl. Acad. Sci. USA 86: 6553-6556 (1989); Lemaitre *et al.*, Proc. Natl. Acad. Sci. USA 84: 648-652 (1987); PCT Publication No. W088/09810) or the blood-brain barrier (see, *e.g.*, PCT Publication No. W089/10134). In addition, oligonucleotides can be modified with hybridization-triggered cleavage agents (See, *e.g.*, Krol *et al.*, Bio-Techniques 6: 958-

976 (1988)) or intercalating agents. (See, *e.g.*, Zon, Pharm. Res. 5: 539-549 (1988)). To this end, the oligonucleotide may be conjugated to another molecule, (*e.g.*, a peptide, hybridization triggered cross-linking agent, transport agent, or hybridization-triggered cleavage agent).

[0148] Also included herein are molecular beacon oligonucleotide primer and probe molecules having one or more regions complementary to a nucleotide sequence of SEQ ID NO: 1-8 or a substantially identical sequence thereof, two complementary regions one having a fluorophore and one a quencher such that the molecular beacon is useful for quantifying the presence of the nucleic acid in a sample. Molecular beacon nucleic acids are described, for example, in Lizardi *et al.*, U.S. Patent No. 5,854,033; Nazarenko *et al.*, U.S. Patent No. 5,866,336, and Livak *et al.*, U.S. Patent 5,876,930.

Antibodies

[0149] The term “antibody” as used herein refers to an immunoglobulin molecule or immunologically active portion thereof, *i.e.*, an antigen-binding portion. Examples of immunologically active portions of immunoglobulin molecules include F(ab) and F(ab')₂ fragments which can be generated by treating the antibody with an enzyme such as pepsin. An antibody sometimes is a polyclonal, monoclonal, recombinant (*e.g.*, a chimeric or humanized), fully human, non-human (*e.g.*, murine), or a single chain antibody. An antibody may have effector function and can fix complement, and is sometimes coupled to a toxin or imaging agent.

[0150] A full-length polypeptide or antigenic peptide fragment encoded by a *DLG1*, *KIAA0783*, *DPF3* or *CENPCI* nucleotide sequence can be used as an immunogen or can be used to identify antibodies made with other immunogens, *e.g.*, cells, membrane preparations, and the like. An antigenic peptide often includes at least 8 amino acid residues of the amino acid sequences encoded by a nucleotide sequence of SEQ ID NO: 1-8, or substantially identical sequence thereof, and encompasses an epitope. Antigenic peptides sometimes include 10 or more amino acids, 15 or more amino acids, 20 or more amino acids, or 30 or more amino acids. Hydrophilic and hydrophobic fragments of polypeptides sometimes are used as immunogens.

[0151] Epitopes encompassed by the antigenic peptide are regions located on the surface of the polypeptide (*e.g.*, hydrophilic regions) as well as regions with high antigenicity. For example, an Emini surface probability analysis of the human polypeptide sequence can be used to indicate the regions that have a particularly high probability of being localized to the surface of the polypeptide and are thus likely to constitute surface residues useful for targeting antibody production. The antibody may bind an epitope on any domain or region on polypeptides described herein.

[0152] Also, chimeric, humanized, and completely human antibodies are useful for applications which include repeated administration to subjects. Chimeric and humanized monoclonal antibodies, comprising both human and non-human portions, can be made using standard recombinant DNA techniques. Such chimeric and humanized monoclonal antibodies can be produced by recombinant

DNA techniques known in the art, for example using methods described in Robinson et al International Application No. PCT/US86/02269; Akira, et al European Patent Application 184,187; Taniguchi, M., European Patent Application 171,496; Morrison et al European Patent Application 173,494; Neuberger et al PCT International Publication No. WO 86/01533; Cabilly et al U.S. Patent No. 4,816,567; Cabilly et al European Patent Application 125,023; Better *et al.*, Science 240: 1041-1043 (1988); Liu *et al.*, Proc. Natl. Acad. Sci. USA 84: 3439-3443 (1987); Liu *et al.*, J. Immunol. 139: 3521-3526 (1987); Sun *et al.*, Proc. Natl. Acad. Sci. USA 84: 214-218 (1987); Nishimura *et al.*, Canc. Res. 47: 999-1005 (1987); Wood *et al.*, Nature 314: 446-449 (1985); and Shaw *et al.*, J. Natl. Cancer Inst. 80: 1553-1559 (1988); Morrison, S. L., Science 229: 1202-1207 (1985); Oi *et al.*, BioTechniques 4: 214 (1986); Winter U.S. Patent 5,225,539; Jones *et al.*, Nature 321: 552-525 (1986); Verhoeyan *et al.*, Science 239: 1534; and Beidler *et al.*, J. Immunol. 141: 4053-4060 (1988).

[0153] Completely human antibodies are particularly desirable for therapeutic treatment of human patients. Such antibodies can be produced using transgenic mice that are incapable of expressing endogenous immunoglobulin heavy and light chains genes, but which can express human heavy and light chain genes. See, for example, Lonberg and Huszar, Int. Rev. Immunol. 13: 65-93 (1995); and U.S. Patent Nos. 5,625,126; 5,633,425; 5,569,825; 5,661,016; and 5,545,806. In addition, companies such as Abgenix, Inc. (Fremont, CA) and Medarex, Inc. (Princeton, NJ), can be engaged to provide human antibodies directed against a selected antigen using technology similar to that described above. Completely human antibodies that recognize a selected epitope also can be generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody (*e.g.*, a murine antibody) is used to guide the selection of a completely human antibody recognizing the same epitope. This technology is described for example by Jespers *et al.*, Bio/Technology 12: 899-903 (1994).

[0154] Antibody can be a single chain antibody. A single chain antibody (scFV) can be engineered (see, *e.g.*, Colcher *et al.*, Ann. N Y Acad. Sci. 880: 263-80 (1999); and Reiter, Clin. Cancer Res. 2: 245-52 (1996)). Single chain antibodies can be dimerized or multimerized to generate multivalent antibodies having specificities for different epitopes of the same target polypeptide.

[0155] Antibodies also may be selected or modified so that they exhibit reduced or no ability to bind an Fc receptor. For example, an antibody may be an isotype or subtype, fragment or other mutant, which does not support binding to an Fc receptor (*e.g.*, it has a mutagenized or deleted Fc receptor binding region).

[0156] Also, an antibody (or fragment thereof) may be conjugated to a therapeutic moiety such as a cytotoxin, a therapeutic agent or a radioactive metal ion. A cytotoxin or cytotoxic agent includes any agent that is detrimental to cells. Examples include taxol, cytochalasin B, gramicidin D, ethidium bromide, emetine, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicin, doxorubicin, daunorubicin, dihydroxy anthracin dione, mitoxantrone, mithramycin, actinomycin D, 1 dehydrotestosterone, glucocorticoids, procaine, tetracaine, lidocaine, propranolol, and puromycin and

analogous or homologs thereof. Therapeutic agents include, but are not limited to, antimetabolites (*e.g.*, methotrexate, 6-mercaptopurine, 6-thioguanine, cytarabine, 5-fluorouracil decarbazine), alkylating agents (*e.g.*, mechlorethamine, thiotepa chlorambucil, melphalan, carmustine (BCNU) and lomustine (CCNU), cyclophosphamide, busulfan, dibromomannitol, streptozotocin, mitomycin C, and cis-dichlorodiamine platinum (II) (DDP) cisplatin), anthracyclines (*e.g.*, daunorubicin (formerly daunomycin) and doxorubicin), antibiotics (*e.g.*, dactinomycin (formerly actinomycin), bleomycin, mithramycin, and anthramycin (AMC)), and anti-mitotic agents (*e.g.*, vincristine and vinblastine).

[0157] Antibody conjugates can be used for modifying a given biological response. For example, the drug moiety may be a protein or polypeptide possessing a desired biological activity. Such proteins may include, for example, a toxin such as abrin, ricin A, pseudomonas exotoxin, or diphtheria toxin; a polypeptide such as tumor necrosis factor, γ -interferon, α -interferon, nerve growth factor, platelet derived growth factor, tissue plasminogen activator; or, biological response modifiers such as, for example, lymphokines, interleukin-1 ("IL-1"), interleukin-2 ("IL-2"), interleukin-6 ("IL-6"), granulocyte macrophage colony stimulating factor ("GM-CSF"), granulocyte colony stimulating factor ("G-CSF"), or other growth factors. Also, an antibody can be conjugated to a second antibody to form an antibody heteroconjugate as described by Segal in U.S. Patent No. 4,676,980, for example.

[0158] An antibody (*e.g.*, monoclonal antibody) can be used to isolate target polypeptides by standard techniques, such as affinity chromatography or immunoprecipitation. Moreover, an antibody can be used to detect a target polypeptide (*e.g.*, in a cellular lysate or cell supernatant) in order to evaluate the abundance and pattern of expression of the polypeptide. Antibodies can be used diagnostically to monitor polypeptide levels in tissue as part of a clinical testing procedure, *e.g.*, to determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling (*i.e.*, physically linking) the antibody to a detectable substance (*i.e.*, antibody labeling). Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, and radioactive materials. Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, β -galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include ^{125}I , ^{131}I , ^{35}S or ^3H . Also, an antibody can be utilized as a test molecule for determining whether it can treat breast cancer, and as a therapeutic for administration to a subject for treating breast cancer.

[0159] An antibody can be made by immunizing with a purified antigen, or a fragment thereof, *e.g.*, a fragment described herein, a membrane associated antigen, tissues, *e.g.*, crude tissue preparations, whole cells, preferably living cells, lysed cells, or cell fractions.

[0160] Included herein are antibodies which bind only a native polypeptide, only denatured or otherwise non-native polypeptide, or which bind both, as well as those having linear or conformational epitopes. Conformational epitopes sometimes can be identified by selecting antibodies that bind to native but not denatured polypeptide. Also featured are antibodies that specifically bind to a polypeptide variant associated with breast cancer.

Screening Assays

[0161] Featured herein are methods for identifying a candidate therapeutic for treating breast cancer. The methods comprise contacting a test molecule with a target molecule in a system. A “target molecule” as used herein refers to a nucleic acid of SEQ ID NO: 1-8, a substantially identical nucleic acid thereof, or a fragment thereof, and an encoded polypeptide of the foregoing. The method also comprises determining the presence or absence of an interaction between the test molecule and the target molecule, where the presence of an interaction between the test molecule and the nucleic acid or polypeptide identifies the test molecule as a candidate breast cancer therapeutic. The interaction between the test molecule and the target molecule may be quantified.

[0162] Test molecules and candidate therapeutics include, but are not limited to, compounds, antisense nucleic acids, siRNA molecules, ribozymes, polypeptides or proteins encoded by a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acids, or a substantially identical sequence or fragment thereof, and immunotherapeutics (*e.g.*, antibodies and HLA-presented polypeptide fragments). A test molecule or candidate therapeutic may act as a modulator of target molecule concentration or target molecule function in a system. A “modulator” may agonize (*i.e.*, up-regulates) or antagonize (*i.e.*, down-regulates) a target molecule concentration partially or completely in a system by affecting such cellular functions as DNA replication and/or DNA processing (*e.g.*, DNA methylation or DNA repair), RNA transcription and/or RNA processing (*e.g.*, removal of intronic sequences and/or translocation of spliced mRNA from the nucleus), polypeptide production (*e.g.*, translation of the polypeptide from mRNA), and/or polypeptide post-translational modification (*e.g.*, glycosylation, phosphorylation, and proteolysis of pro-polypeptides). A modulator may also agonize or antagonize a biological function of a target molecule partially or completely, where the function may include adopting a certain structural conformation, interacting with one or more binding partners, ligand binding, catalysis (*e.g.*, phosphorylation, dephosphorylation, hydrolysis, methylation, and isomerization), and an effect upon a cellular event (*e.g.*, effecting progression of breast cancer).

[0163] As used herein, the term “system” refers to a cell free *in vitro* environment and a cell-based environment such as a collection of cells, a tissue, an organ, or an organism. A system is “contacted” with a test molecule in a variety of manners, including adding molecules in solution and allowing them to interact with one another by diffusion, cell injection, and any administration routes in an animal. As used herein, the term “interaction” refers to an effect of a test molecule on test

molecule, where the effect sometimes is binding between the test molecule and the target molecule, and sometimes is an observable change in cells, tissue, or organism.

[0164] There are many standard methods for detecting the presence or absence of an interaction between a test molecule and a target molecule. For example, titrametric, acidimetric, radiometric, NMR, monolayer, polarographic, spectrophotometric, fluorescent, and ESR assays probative of a target molecule interaction may be utilized.

[0165] In general, an interaction can be determined by labeling the test molecule and/or the *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* molecule, where the label is covalently or non-covalently attached to the test molecule or *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* molecule. The label is sometimes a radioactive molecule such as ^{125}I , ^{131}I , ^{35}S or ^3H , which can be detected by direct counting of radioemission or by scintillation counting. Also, enzymatic labels such as horseradish peroxidase, alkaline phosphatase, or luciferase may be utilized where the enzymatic label can be detected by determining conversion of an appropriate substrate to product. Also, presence or absence of an interaction can be determined without labeling. For example, a microphysiometer (e.g., Cytosensor) is an analytical instrument that measures the rate at which a cell acidifies its environment using a light-addressable potentiometric sensor (LAPS). Changes in this acidification rate can be used as an indication of an interaction between a test molecule and *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* (McConnell, H. M. et al., Science 257: 1906-1912 (1992)).

[0166] In cell-based systems, cells typically include a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acid or polypeptide or variants thereof and are often of mammalian origin, although the cell can be of any origin. Whole cells, cell homogenates, and cell fractions (e.g., cell membrane fractions) can be subjected to analysis. Where interactions between a test molecule with a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide or variant thereof are monitored, soluble and/or membrane bound forms of the polypeptide or variant may be utilized. Where membrane-bound forms of the polypeptide are used, it may be desirable to utilize a solubilizing agent. Examples of such solubilizing agents include non-ionic detergents such as n-octylglucoside, n-dodecylglucoside, n-dodecylmaltoside, octanoyl-N-methylglucamide, decanoyl-N-methylglucamide, Triton[®] X-100, Triton[®] X-114, Thesit[®], Isotridecypoly(ethylene glycol ether)_n, 3-[(3-cholamidopropyl)dimethylamminio]-1-propane sulfonate (CHAPS), 3-[(3-cholamidopropyl)dimethylamminio]-2-hydroxy-1-propane sulfonate (CHAPSO), or N-dodecyl-N,N-dimethyl-3-ammonio-1-propane sulfonate.

[0167] An interaction between two molecules also can be detected by monitoring fluorescence energy transfer (FET) (see, for example, Lakowicz et al., U.S. Patent No. 5,631,169; Stavrianopoulos et al. U.S. Patent No. 4,868,103). A fluorophore label on a first, "donor" molecule is selected such that its emitted fluorescent energy will be absorbed by a fluorescent label on a second, "acceptor" molecule, which in turn is able to fluoresce due to the absorbed energy. Alternately, the "donor" polypeptide molecule may simply utilize the natural fluorescent energy of tryptophan residues.

Labels are chosen that emit different wavelengths of light, such that the “acceptor” molecule label may be differentiated from that of the “donor”. Since the efficiency of energy transfer between the labels is related to the distance separating the molecules, the spatial relationship between the molecules can be assessed. In a situation in which binding occurs between the molecules, the fluorescent emission of the “acceptor” molecule label in the assay should be maximal. An FET binding event can be conveniently measured through standard fluorometric detection means well known in the art (e.g., using a fluorimeter).

[0168] In another embodiment, determining the presence or absence of an interaction between a test molecule and a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* molecule can be effected by using real-time Biomolecular Interaction Analysis (BIA) (see, e.g., Sjolander & Urbanicz, Anal. Chem. 63: 2338-2345 (1991) and Szabo et al., Curr. Opin. Struct. Biol. 5: 699-705 (1995)). “Surface plasmon resonance” or “BIA” detects biospecific interactions in real time, without labeling any of the interactants (e.g., BIAcore). Changes in the mass at the binding surface (indicative of a binding event) result in alterations of the refractive index of light near the surface (the optical phenomenon of surface plasmon resonance (SPR)), resulting in a detectable signal which can be used as an indication of real-time reactions between biological molecules.

[0169] In another embodiment, the *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* molecule or test molecules are anchored to a solid phase. The *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* molecule/test molecule complexes anchored to the solid phase can be detected at the end of the reaction. The target *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* molecule is often anchored to a solid surface, and the test molecule, which is not anchored, can be labeled, either directly or indirectly, with detectable labels discussed herein.

[0170] It may be desirable to immobilize a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* molecule, an anti-*DLG1*, *KIAA0783*, *DPF3* or *CENPC1* antibody, or test molecules to facilitate separation of complexed from uncomplexed forms of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* molecules and test molecules, as well as to accommodate automation of the assay. Binding of a test molecule to a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* molecule can be accomplished in any vessel suitable for containing the reactants. Examples of such vessels include microtiter plates, test tubes, and micro-centrifuge tubes. In one embodiment, a fusion polypeptide can be provided which adds a domain that allows a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* molecule to be bound to a matrix. For example, glutathione-S-transferase/*DLG1*, *KIAA0783*, *DPF3* or *CENPC1* fusion polypeptides or glutathione-S-transferase/target fusion polypeptides can be adsorbed onto glutathione sepharose beads (Sigma Chemical, St. Louis, MO) or glutathione derivitized microtiter plates, which are then combined with the test compound or the test compound and either the non-adsorbed target polypeptide or *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide, and the mixture incubated under conditions conducive to complex formation (e.g., at physiological conditions for salt and pH). Following incubation, the beads or microtiter plate wells are washed to remove any unbound components, the matrix

immobilized in the case of beads, complex determined either directly or indirectly, for example, as described above. Alternatively, the complexes can be dissociated from the matrix, and the level of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* binding or activity determined using standard techniques.

[0171] Other techniques for immobilizing a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* molecule on matrices include using biotin and streptavidin. For example, biotinylated *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide or target molecules can be prepared from biotin-NHS (N-hydroxy-succinimide) using techniques known in the art (e.g., biotinylation kit, Pierce Chemicals, Rockford, IL), and immobilized in the wells of streptavidin-coated 96 well plates (Pierce Chemical).

[0172] In order to conduct the assay, the non-immobilized component is added to the coated surface containing the anchored component. After the reaction is complete, unreacted components are removed (e.g., by washing) under conditions such that any complexes formed will remain immobilized on the solid surface. The detection of complexes anchored on the solid surface can be accomplished in a number of ways. Where the previously non-immobilized component is pre-labeled, the detection of label immobilized on the surface indicates that complexes were formed. Where the previously non-immobilized component is not pre-labeled, an indirect label can be used to detect complexes anchored on the surface; e.g., using a labeled antibody specific for the immobilized component (the antibody, in turn, can be directly labeled or indirectly labeled with, e.g., a labeled anti-Ig antibody).

[0173] In one embodiment, this assay is performed utilizing antibodies reactive with *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide or test molecules but which do not interfere with binding of the *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide to its test molecule. Such antibodies can be derivitized to the wells of the plate, and unbound target or *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide trapped in the wells by antibody conjugation. Methods for detecting such complexes, in addition to those described above for the GST-immobilized complexes, include immunodetection of complexes using antibodies reactive with the *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide or target molecule, as well as enzyme-linked assays which rely on detecting an enzymatic activity associated with the *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide or test molecule.

[0174] Alternatively, cell free assays can be conducted in a liquid phase. In such an assay, the reaction products are separated from unreacted components, by any of a number of standard techniques, including but not limited to: differential centrifugation (see, for example, Rivas, G., and Minton, A. P., Trends Biochem Sci Aug;18(8): 284-7 (1993)); chromatography (gel filtration chromatography, ion-exchange chromatography); electrophoresis (see, e.g., Ausubel et al., eds. Current Protocols in Molecular Biology, J. Wiley: New York (1999)); and immunoprecipitation (see, for example, Ausubel, F. et al., eds. Current Protocols in Molecular Biology, J. Wiley: New York (1999)). Such resins and chromatographic techniques are known to one skilled in the art (see, e.g., Heegaard, J Mol. Recognit. Winter; 11(1-6): 141-8 (1998); Hage & Tweed, J. Chromatogr. B Biomed. Sci. Appl. Oct 10; 699 (1-2): 499-525 (1997)). Further, fluorescence energy transfer may

also be conveniently utilized, as described herein, to detect binding without further purification of the complex from solution.

[0175] In another embodiment, modulators of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* expression are identified. For example, a cell or cell free mixture is contacted with a candidate compound and the expression of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* mRNA or polypeptide evaluated relative to the level of expression of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* mRNA or polypeptide in the absence of the candidate compound. When expression of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* mRNA or polypeptide is greater in the presence of the candidate compound than in its absence, the candidate compound is identified as a stimulator of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* mRNA or polypeptide expression. Alternatively, when expression of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* mRNA or polypeptide is less (statistically significantly less) in the presence of the candidate compound than in its absence, the candidate compound is identified as an inhibitor of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* mRNA or polypeptide expression. The level of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* mRNA or polypeptide expression can be determined by methods described herein for detecting *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* mRNA or polypeptide.

[0176] In another embodiment, binding partners that interact with a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* molecule are detected. The *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* molecules can interact with one or more cellular or extracellular macromolecules, such as polypeptides, in vivo, and these molecules that interact with *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* molecules are referred to herein as "binding partners." Molecules that disrupt such interactions can be useful in regulating the activity of the target gene product. Such molecules can include, but are not limited to molecules such as antibodies, peptides, and small molecules. Target genes/products for use in this embodiment often are the *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* genes herein identified. In an alternative embodiment, provided is a method for determining the ability of the test compound to modulate the activity of a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide through modulation of the activity of a downstream effector of a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* target molecule. For example, the activity of the effector molecule on an appropriate target can be determined, or the binding of the effector to an appropriate target can be determined, as previously described.

[0177] To identify compounds that interfere with the interaction between the target gene product and its cellular or extracellular binding partner(s), e.g., a substrate, a reaction mixture containing the target gene product and the binding partner is prepared, under conditions and for a time sufficient, to allow the two products to form complex. In order to test an inhibitory agent, the reaction mixture is provided in the presence and absence of the test compound. The test compound can be initially included in the reaction mixture, or can be added at a time subsequent to the addition of the target gene and its cellular or extracellular binding partner. Control reaction mixtures are incubated without the test compound or with a placebo. The formation of any complexes between the target gene product and the cellular or extracellular binding partner is then detected. The formation of a complex

in the control reaction, but not in the reaction mixture containing the test compound, indicates that the compound interferes with the interaction of the target gene product and the interactive binding partner. Additionally, complex formation within reaction mixtures containing the test compound and normal target gene product can also be compared to complex formation within reaction mixtures containing the test compound and mutant target gene product. This comparison can be important in those cases where it is desirable to identify compounds that disrupt interactions of mutant but not normal target gene products.

[0178] These assays can be conducted in a heterogeneous or homogeneous format.

Heterogeneous assays involve anchoring either the target gene product or the binding partner onto a solid phase, and detecting complexes anchored on the solid phase at the end of the reaction. In homogeneous assays, the entire reaction is carried out in a liquid phase. In either approach, the order of addition of reactants can be varied to obtain different information about the compounds being tested. For example, test compounds that interfere with the interaction between the target gene products and the binding partners, e.g., by competition, can be identified by conducting the reaction in the presence of the test substance. Alternatively, test compounds that disrupt preformed complexes, e.g., compounds with higher binding constants that displace one of the components from the complex, can be tested by adding the test compound to the reaction mixture after complexes have been formed. The various formats are briefly described below.

[0179] In a heterogeneous assay system, either the target gene product or the interactive cellular or extracellular binding partner, is anchored onto a solid surface (e.g., a microtiter plate), while the non-anchored species is labeled, either directly or indirectly. The anchored species can be immobilized by non-covalent or covalent attachments. Alternatively, an immobilized antibody specific for the species to be anchored can be used to anchor the species to the solid surface.

[0180] In order to conduct the assay, the partner of the immobilized species is exposed to the coated surface with or without the test compound. After the reaction is complete, unreacted components are removed (e.g., by washing) and any complexes formed will remain immobilized on the solid surface. Where the non-immobilized species is pre-labeled, the detection of label immobilized on the surface indicates that complexes were formed. Where the non-immobilized species is not pre-labeled, an indirect label can be used to detect complexes anchored on the surface; e.g., using a labeled antibody specific for the initially non-immobilized species (the antibody, in turn, can be directly labeled or indirectly labeled with, e.g., a labeled anti-Ig antibody). Depending upon the order of addition of reaction components, test compounds that inhibit complex formation or that disrupt preformed complexes can be detected.

[0181] Alternatively, the reaction can be conducted in a liquid phase in the presence or absence of the test compound, the reaction products separated from unreacted components, and complexes detected; e.g., using an immobilized antibody specific for one of the binding components to anchor any complexes formed in solution, and a labeled antibody specific for the other partner to detect

anchored complexes. Again, depending upon the order of addition of reactants to the liquid phase, test compounds that inhibit complex or that disrupt preformed complexes can be identified.

[0182] In an alternate embodiment, a homogeneous assay can be used. For example, a preformed complex of the target gene product and the interactive cellular or extracellular binding partner product is prepared in that either the target gene products or their binding partners are labeled, but the signal generated by the label is quenched due to complex formation (see, e.g., U.S. Patent No. 4,109,496 that utilizes this approach for immunoassays). The addition of a test substance that competes with and displaces one of the species from the preformed complex will result in the generation of a signal above background. In this way, test substances that disrupt target gene product-binding partner interaction can be identified.

[0183] Also, binding partners of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* molecules can be identified in a two-hybrid assay or three-hybrid assay (see, e.g., U.S. Patent No. 5,283,317; Zervos et al., Cell 72:223-232 (1993); Madura et al., J. Biol. Chem. 268: 12046-12054 (1993); Bartel et al., Biotechniques 14: 920-924 (1993); Iwabuchi et al., Oncogene 8: 1693-1696 (1993); and Brent WO94/10300), to identify other polypeptides, which bind to or interact with *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* ("*DLG1*, *KIAA0783*, *DPF3* or *CENPC1*-binding polypeptides" or "*DLG1*, *KIAA0783*, *DPF3* or *CENPC1*-bp") and are involved in *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* activity. Such *DLG1*, *KIAA0783*, *DPF3* or *CENPC1*-bps can be activators or inhibitors of signals by the *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptides or *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* targets as, for example, downstream elements of a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1*-mediated signaling pathway.

[0184] A two-hybrid system is based on the modular nature of most transcription factors, which consist of separable DNA-binding and activation domains. Briefly, the assay utilizes two different DNA constructs. In one construct, the gene that codes for a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide is fused to a gene encoding the DNA binding domain of a known transcription factor (e.g., GAL-4). In the other construct, a DNA sequence, from a library of DNA sequences, that encodes an unidentified polypeptide ("prey" or "sample") is fused to a gene that codes for the activation domain of the known transcription factor. (Alternatively the: *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide can be the fused to the activator domain.) If the "bait" and the "prey" polypeptides are able to interact, in vivo, forming a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1*-dependent complex, the DNA-binding and activation domains of the transcription factor are brought into close proximity. This proximity allows transcription of a reporter gene (e.g., LacZ) which is operably linked to a transcriptional regulatory site responsive to the transcription factor. Expression of the reporter gene can be detected and cell colonies containing the functional transcription factor can be isolated and used to obtain the cloned gene which encodes the polypeptide which interacts with the *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide.

[0185] Candidate therapeutics for treating breast cancer are identified from a group of test molecules that interact with a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acid or polypeptide. Test molecules are normally ranked according to the degree with which they interact or modulate (e.g., agonize or antagonize) DNA replication and/or processing, RNA transcription and/or processing, polypeptide production and/or processing, and/or function of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* molecules, for example, and then top ranking modulators are selected. In a preferred embodiment, the candidate therapeutic (i.e., test molecule) acts as a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* antagonist. Also, pharmacogenomic information described herein can determine the rank of a modulator. Candidate therapeutics typically are formulated for administration to a subject.

Therapeutic Treatments

[0186] Formulations or pharmaceutical compositions typically include in combination with a pharmaceutically acceptable carrier, a compound, an antisense nucleic acid, a ribozyme, an antibody, a binding partner that interacts with a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide, a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acid, or a fragment thereof. The formulated molecule may be one that is identified by a screening method described above. Also, formulations may comprise a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide or fragment thereof. As used herein, the term “pharmaceutically acceptable carrier” includes solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like, compatible with pharmaceutical administration. Supplementary active compounds can also be incorporated into the compositions.

[0187] A pharmaceutical composition is formulated to be compatible with its intended route of administration. Examples of routes of administration include parenteral, e.g., intravenous, intradermal, subcutaneous, oral (e.g., inhalation), transdermal (topical), transmucosal, and rectal administration. Solutions or suspensions used for parenteral, intradermal, or subcutaneous application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerin, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as acetates, citrates or phosphates and agents for the adjustment of tonicity such as sodium chloride or dextrose. pH can be adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide. The parenteral preparation can be enclosed in ampoules, disposable syringes or multiple dose vials made of glass or plastic.

[0188] Oral compositions generally include an inert diluent or an edible carrier. For the purpose of oral therapeutic administration, the active compound can be incorporated with excipients and used in the form of tablets, troches, or capsules, e.g., gelatin capsules. Oral compositions can also be

prepared using a fluid carrier for use as a mouthwash. Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition. The tablets, pills, capsules, troches and the like can contain any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or Sterotes; a glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

[0189] Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL™ (BASF, Parsippany, NJ) or phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be fluid to the extent that easy syringability exists. It should be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, and the like. In many cases, isotonic agents, for example, sugars, polyalcohols such as mannitol, sorbitol, sodium chloride sometimes are included in the composition. Prolonged absorption of the injectable compositions can be brought about by including in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

[0190] Sterile injectable solutions can be prepared by incorporating the active compound in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle which contains a basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, methods of preparation often utilized are vacuum drying and freeze-drying which yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

[0191] For administration by inhalation, the compounds are delivered in the form of an aerosol spray from pressured container or dispenser which contains a suitable propellant, e.g., a gas such as carbon dioxide, or a nebulizer.

[0192] Systemic administration can also be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are

used in the formulation. Such penetrants are generally known in the art, and include, for example, for transmucosal administration, detergents, bile salts, and fusidic acid derivatives. Transmucosal administration can be accomplished through the use of nasal sprays or suppositories. For transdermal administration, the active compounds are formulated into ointments, salves, gels, or creams as generally known in the art. Molecules can also be prepared in the form of suppositories (e.g., with conventional suppository bases such as cocoa butter and other glycerides) or retention enemas for rectal delivery.

[0193] In one embodiment, active molecules are prepared with carriers that will protect the compound against rapid elimination from the body, such as a controlled release formulation, including implants and microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Methods for preparation of such formulations will be apparent to those skilled in the art. Materials can also be obtained commercially from Alza Corporation and Nova Pharmaceuticals, Inc. Liposomal suspensions (including liposomes targeted to infected cells with monoclonal antibodies to viral antigens) can also be used as pharmaceutically acceptable carriers. These can be prepared according to methods known to those skilled in the art, for example, as described in U.S. Patent No. 4,522,811.

[0194] It is advantageous to formulate oral or parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the subject to be treated; each unit containing a predetermined quantity of active compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier.

[0195] Toxicity and therapeutic efficacy of such compounds can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, e.g., for determining the LD₅₀ (the dose lethal to 50% of the population) and the ED₅₀ (the dose therapeutically effective in 50% of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index and it can be expressed as the ratio LD₅₀/ED₅₀. Molecules which exhibit high therapeutic indices often are utilized. While molecules that exhibit toxic side effects may be used, care should be taken to design a delivery system that targets such compounds to the site of affected tissue in order to minimize potential damage to uninfected cells and, thereby, reduce side effects.

[0196] The data obtained from the cell culture assays and animal studies can be used in formulating a range of dosage for use in humans. The dosage of such molecules often lies within a range of circulating concentrations that include the ED₅₀ with little or no toxicity. The dosage may vary within this range depending upon the dosage form employed and the route of administration utilized. For any molecules used in the methods described herein, the therapeutically effective dose can be estimated initially from cell culture assays. A dose may be formulated in animal models to achieve a circulating plasma concentration range that includes the IC₅₀ (i.e., the concentration of the

test compound which achieves a half-maximal inhibition of symptoms) as determined in cell culture. Such information can be used to more accurately determine useful doses in humans. Levels in plasma may be measured, for example, by high performance liquid chromatography.

[0197] As defined herein, a therapeutically effective amount of protein or polypeptide (i.e., an effective dosage) ranges from about 0.001 to 30 mg/kg body weight, sometimes about 0.01 to 25 mg/kg body weight, often about 0.1 to 20 mg/kg body weight, and more often about 1 to 10 mg/kg, 2 to 9 mg/kg, 3 to 8 mg/kg, 4 to 7 mg/kg, or 5 to 6 mg/kg body weight. The protein or polypeptide can be administered one time per week for between about 1 to 10 weeks, sometimes between 2 to 8 weeks, often between about 3 to 7 weeks, and more often for about 4, 5, or 6 weeks. The skilled artisan will appreciate that certain factors may influence the dosage and timing required to effectively treat a subject, including but not limited to the severity of the disease or disorder, previous treatments, the general health and/or age of the subject, and other diseases present. Moreover, treatment of a subject with a therapeutically effective amount of a protein, polypeptide, or antibody can include a single treatment, or sometimes can include a series of treatments.

[0198] With regard to polypeptide formulations, featured herein is a method for treating breast cancer in a subject, which comprises contacting one or more cells in the subject with a first *DLG1*, *KIAA0783*, *DPF3* or *CENPCI* polypeptide, where the subject comprises a second *DLG1*, *KIAA0783*, *DPF3* or *CENPCI* polypeptide having one or more polymorphic variations associated with cancer, and where the first polypeptide comprises fewer polymorphic variations associated with cancer than the second polypeptide. The first and second polypeptides are encoded by a nucleic acid which comprises a nucleotide sequence selected from the group consisting of the nucleotide sequence of SEQ ID NO: 1-8; a nucleotide sequence which encodes a polypeptide consisting of an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 1-8; a nucleotide sequence which encodes a polypeptide that is 90% or more identical to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 1-8 and a nucleotide sequence 90% or more identical to a nucleotide sequence of SEQ ID NO: 1-8. The subject is often a human.

[0199] For antibodies, a dosage of 0.1 mg/kg of body weight (generally 10 mg/kg to 20 mg/kg) is often utilized. If the antibody is to act in the brain, a dosage of 50 mg/kg to 100 mg/kg is often appropriate. Generally, partially human antibodies and fully human antibodies have a longer half-life within the human body than other antibodies. Accordingly, lower dosages and less frequent administration is often possible. Modifications such as lipidation can be used to stabilize antibodies and to enhance uptake and tissue penetration (e.g., into the brain). A method for lipidation of antibodies is described by Cruikshank et al., J. Acquired Immune Deficiency Syndromes and Human Retrovirology 14:193 (1997).

[0200] Antibody conjugates can be used for modifying a given biological response, the drug moiety is not to be construed as limited to classical chemical therapeutic agents. For example, the drug moiety may be a protein or polypeptide possessing a desired biological activity. Such proteins

may include, for example, a toxin such as abrin, ricin A, pseudomonas exotoxin, or diphtheria toxin; a polypeptide such as tumor necrosis factor, .alpha.-interferon, .beta.-interferon, nerve growth factor, platelet derived growth factor, tissue plasminogen activator; or, biological response modifiers such as, for example, lymphokines, interleukin-1 ("IL-1"), interleukin-2 ("IL-2"), interleukin-6 ("IL-6"), granulocyte macrophage colony stimulating factor ("GM-CSF"), granulocyte colony stimulating factor ("G-CSF"), or other growth factors. Alternatively, an antibody can be conjugated to a second antibody to form an antibody heteroconjugate as described by Segal in U.S. Patent No. 4,676,980.

[0201] For compounds, exemplary doses include milligram or microgram amounts of the compound per kilogram of subject or sample weight, for example, about 1 microgram per kilogram to about 500 milligrams per kilogram, about 100 micrograms per kilogram to about 5 milligrams per kilogram, or about 1 microgram per kilogram to about 50 micrograms per kilogram. It is understood that appropriate doses of a small molecule depend upon the potency of the small molecule with respect to the expression or activity to be modulated. When one or more of these small molecules is to be administered to an animal (e.g., a human) in order to modulate expression or activity of a polypeptide or nucleic acid described herein, a physician, veterinarian, or researcher may, for example, prescribe a relatively low dose at first, subsequently increasing the dose until an appropriate response is obtained. In addition, it is understood that the specific dose level for any particular animal subject will depend upon a variety of factors including the activity of the specific compound employed, the age, body weight, general health, gender, and diet of the subject, the time of administration, the route of administration, the rate of excretion, any drug combination, and the degree of expression or activity to be modulated.

[0202] *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acid molecules can be inserted into vectors and used in gene therapy methods for treating breast cancer. Featured herein is a method for treating breast cancer in a subject, which comprises contacting one or more cells in the subject with a first *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acid, where genomic DNA in the subject comprises a second *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acid comprising one or more polymorphic variations associated with breast cancer, and where the first *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acid comprises fewer polymorphic variations associated with breast cancer. The first and second nucleic acids typically comprise a nucleotide sequence selected from the group consisting of the nucleotide sequence of SEQ ID NO: 1-8; a nucleotide sequence which encodes a polypeptide consisting of an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 1-8; a nucleotide sequence that is 90% or more identical to the nucleotide sequence of SEQ ID NO: 1-8, and a nucleotide sequence which encodes a polypeptide that is 90% or more identical to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 1-8. The subject often is a human.

[0203] Gene therapy vectors can be delivered to a subject by, for example, intravenous injection, local administration (see U.S. Patent 5,328,470) or by stereotactic injection (see e.g., Chen et al., (1994) Proc. Natl. Acad. Sci. USA 91:3054-3057). Pharmaceutical preparations of gene therapy

vectors can include a gene therapy vector in an acceptable diluent, or can comprise a slow release matrix in which the gene delivery vehicle is imbedded. Alternatively, where the complete gene delivery vector can be produced intact from recombinant cells (e.g., retroviral vectors) the pharmaceutical preparation can include one or more cells which produce the gene delivery system. Examples of gene delivery vectors are described herein.

[0204] Pharmaceutical compositions can be included in a container, pack, or dispenser together with instructions for administration.

[0205] Pharmaceutical compositions of active ingredients can be administered by any of the paths described herein for therapeutic and prophylactic methods for treating breast cancer. With regard to both prophylactic and therapeutic methods of treatment, such treatments may be specifically tailored or modified, based on knowledge obtained from pharmacogenomic analyses described herein. As used herein, the term "treatment" is defined as the application or administration of a therapeutic agent to a patient, or application or administration of a therapeutic agent to an isolated tissue or cell line from a patient, who has a disease, a symptom of disease or a predisposition toward a disease, with the purpose to cure, heal, alleviate, relieve, alter, remedy, ameliorate, improve or affect the disease, the symptoms of disease or the predisposition toward disease. A therapeutic agent includes, but is not limited to, small molecules, peptides, antibodies, ribozymes and antisense oligonucleotides.

[0206] Administration of a prophylactic agent can occur prior to the manifestation of symptoms characteristic of the *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* aberrance, such that a disease or disorder is prevented or, alternatively, delayed in its progression. Depending on the type of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* aberrance, for example, a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* molecule, *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* agonist, or *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* antagonist agent can be used for treating the subject. The appropriate agent can be determined based on screening assays described herein.

[0207] As discussed, successful treatment of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* disorders can be brought about by techniques that serve to inhibit the expression or activity of target gene products. For example, compounds (e.g., an agent identified using an assays described above) that exhibit negative modulatory activity can be used to prevent and/or treat breast cancer. Such molecules can include, but are not limited to peptides, phosphopeptides, small organic or inorganic molecules, or antibodies (including, for example, polyclonal, monoclonal, humanized, anti-idiotypic, chimeric or single chain antibodies, and FAb, F(ab')₂ and FAb expression library fragments, scFV molecules, and epitope-binding fragments thereof).

[0208] Further, antisense and ribozyme molecules that inhibit expression of the target gene can also be used to reduce the level of target gene expression, thus effectively reducing the level of target gene activity. Still further, triple helix molecules can be utilized in reducing the level of target gene activity. Antisense, ribozyme and triple helix molecules are discussed above.

[0209] It is possible that the use of antisense, ribozyme, and/or triple helix molecules to reduce or inhibit mutant gene expression can also reduce or inhibit the transcription (triple helix) and/or translation (antisense, ribozyme) of mRNA produced by normal target gene alleles, such that the concentration of normal target gene product present can be lower than is necessary for a normal phenotype. In such cases, nucleic acid molecules that encode and express target gene polypeptides exhibiting normal target gene activity can be introduced into cells via gene therapy method. Alternatively, in instances where the target gene encodes an extracellular polypeptide, normal target gene polypeptide often is co-administered into the cell or tissue to maintain the requisite level of cellular or tissue target gene activity.

[0210] Another method by which nucleic acid molecules may be utilized in treating or preventing a disease characterized by *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* expression is through the use of aptamer molecules specific for *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide. Aptamers are nucleic acid molecules having a tertiary structure which permits them to specifically bind to polypeptide ligands (see, e.g., Osborne, et al., Curr. Opin. Chem. Biol.1(1): 5-9 (1997); and Patel, D. J., Curr. Opin. Chem. Biol. Jun;1(1): 32-46 (1997)). Since nucleic acid molecules may in many cases be more conveniently introduced into target cells than therapeutic polypeptide molecules may be, aptamers offer a method by which *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide activity may be specifically decreased without the introduction of drugs or other molecules which may have pluripotent effects.

[0211] Antibodies can be generated that are both specific for target gene product and that reduce target gene product activity. Such antibodies may, therefore, be administered in instances whereby negative modulatory techniques are appropriate for the treatment of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* disorders. For a description of antibodies, see the Antibody section above.

[0212] In circumstances where injection of an animal or a human subject with a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide or epitope for stimulating antibody production is harmful to the subject, it is possible to generate an immune response against *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* through the use of anti-idiotypic antibodies (see, for example, Herlyn, D., Ann. Med.;31(1): 66-78 (1999); and Bhattacharya-Chatterjee & Foon, Cancer Treat. Res.; 94: 51-68 (1998)). If an anti-idiotypic antibody is introduced into a mammal or human subject, it should stimulate the production of anti-anti-idiotypic antibodies, which should be specific to the *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide. Vaccines directed to a disease characterized by *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* expression may also be generated in this fashion.

[0213] In instances where the target antigen is intracellular and whole antibodies are used, internalizing antibodies may be utilized. Lipofectin or liposomes can be used to deliver the antibody or a fragment of the Fab region that binds to the target antigen into cells. Where fragments of the antibody are used, the smallest inhibitory fragment that binds to the target antigen often is utilized. For example, peptides having an amino acid sequence corresponding to the Fv region of the antibody

can be used. Alternatively, single chain neutralizing antibodies that bind to intracellular target antigens can also be administered. Such single chain antibodies can be administered, for example, by expressing nucleotide sequences encoding single-chain antibodies within the target cell population (see e.g., Marasco et al., Proc. Natl. Acad. Sci. USA 90: 7889-7893 (1993)).

[0214] *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* molecules and compounds that inhibit target gene expression, synthesis and/or activity can be administered to a patient at therapeutically effective doses to prevent, treat or ameliorate *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* disorders. A therapeutically effective dose refers to that amount of the compound sufficient to result in amelioration of symptoms of the disorders.

[0215] Toxicity and therapeutic efficacy of such compounds can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, e.g., for determining the LD₅₀ (the dose lethal to 50% of the population) and the ED₅₀ (the dose therapeutically effective in 50% of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index and it can be expressed as the ratio LD₅₀/ED₅₀. Compounds that exhibit large therapeutic indices often are utilized. While compounds that exhibit toxic side effects can be used, care should be taken to design a delivery system that targets such compounds to the site of affected tissue in order to minimize potential damage to uninfected cells and, thereby, reduce side effects.

[0216] Data obtained from cell culture assays and animal studies can be used in formulating a range of dosage for use in humans. The dosage of such compounds often lies within a range of circulating concentrations that include the ED₅₀ with little or no toxicity. The dosage can vary within this range depending upon the dosage form employed and the route of administration utilized. For any compound used in a method described herein, the therapeutically effective dose can be estimated initially from cell culture assays. A dose can be formulated in animal models to achieve a circulating plasma concentration range that includes the IC₅₀ (i.e., the concentration of the test compound that achieves a half-maximal inhibition of symptoms) as determined in cell culture. Such information can be used to more accurately determine useful doses in humans. Levels in plasma can be measured, for example, by high performance liquid chromatography.

[0217] Another example of effective dose determination for an individual is the ability to directly assay levels of “free” and “bound” compound in the serum of the test subject. Such assays may utilize antibody mimics and/or “biosensors” that have been created through molecular imprinting techniques. The compound which is able to modulate *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* activity is used as a template, or “imprinting molecule”, to spatially organize polymerizable monomers prior to their polymerization with catalytic reagents. The subsequent removal of the imprinted molecule leaves a polymer matrix which contains a repeated “negative image” of the compound and is able to selectively rebind the molecule under biological assay conditions. A detailed review of this technique can be seen in Ansell et al., Current Opinion in Biotechnology 7: 89-94 (1996) and in Shea, Trends in Polymer Science 2: 166-173 (1994). Such “imprinted” affinity matrixes are amenable to ligand-

binding assays, whereby the immobilized monoclonal antibody component is replaced by an appropriately imprinted matrix. An example of the use of such matrixes in this way can be seen in Vlatakis, et al., Nature 361: 645-647 (1993). Through the use of isotope-labeling, the “free” concentration of compound which modulates the expression or activity of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* can be readily monitored and used in calculations of IC_{50} . Such “imprinted” affinity matrixes can also be designed to include fluorescent groups whose photon-emitting properties measurably change upon local and selective binding of target compound. These changes can be readily assayed in real time using appropriate fiberoptic devices, in turn allowing the dose in a test subject to be quickly optimized based on its individual IC_{50} . A rudimentary example of such a “biosensor” is discussed in Kriz et al., Analytical Chemistry 67: 2142-2144 (1995).

[0218] Provided herein are methods of modulating *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* expression or activity for therapeutic purposes. Accordingly, in an exemplary embodiment, the modulatory method involves contacting a cell with a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* or agent that modulates one or more of the activities of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide activity associated with the cell. An agent that modulates *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide activity can be an agent as described herein, such as a nucleic acid or a polypeptide, a naturally-occurring target molecule of a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide (e.g., a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* substrate or receptor), a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* antibody, a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* agonist or antagonist, a peptidomimetic of a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* agonist or antagonist, or other small molecule.

[0219] In one embodiment, the agent stimulates one or more *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* activities. Examples of such stimulatory agents include active *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide and a nucleic acid molecule encoding *DLG1*, *KIAA0783*, *DPF3* or *CENPC1*. In another embodiment, the agent inhibits one or more *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* activities. Examples of such inhibitory agents include antisense *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* nucleic acid molecules, anti-*DLG1*, *KIAA0783*, *DPF3* or *CENPC1* antibodies, and *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* inhibitors. These modulatory methods can be performed in vitro (e.g., by culturing the cell with the agent) or, alternatively, in vivo (e.g., by administering the agent to a subject). As such, provided are methods of treating an individual afflicted with a disease or disorder characterized by aberrant or unwanted expression or activity of a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polypeptide or nucleic acid molecule. In one embodiment, the method involves administering an agent (e.g., an agent identified by a screening assay described herein), or combination of agents that modulates (e.g., upregulates or downregulates) *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* expression or activity. In a preferred embodiment, the method involves administering an agent (e.g., an agent identified by a screening assay described herein), or combination of agents that inhibits *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* expression or activity. In another embodiment, the method involves administering a *DLG1*,

KIAA0783, *DPF3* or *CENPC1* polypeptide or nucleic acid molecule as therapy to compensate for reduced, aberrant, or unwanted *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* expression or activity.

[0220] Stimulation of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* activity is desirable in situations in which *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* is abnormally downregulated and/or in which increased *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* activity is likely to have a beneficial effect. For example, stimulation of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* activity is desirable in situations in which a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* is downregulated and/or in which increased *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* activity is likely to have a beneficial effect. Likewise, inhibition of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* activity is desirable in situations in which *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* is abnormally upregulated and/or in which decreased *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* activity is likely to have a beneficial effect.

Methods of Treatment

[0221] In another aspect, provided are methods for identifying a risk of cancer in an individual as described herein and, if a genetic predisposition is identified, treating that individual to delay or reduce or prevent the development of cancer. Such a procedure can be used to treat breast cancer. Optionally, treating an individual for cancer may include inhibiting cellular proliferation, inhibiting metastasis, inhibiting invasion, or preventing tumor formation or growth as defined herein. Suitable treatments to prevent or reduce or delay breast cancer focus on inhibiting additional cellular proliferation, inhibiting metastasis, inhibiting invasion, and preventing further tumor formation or growth. Treatment usually includes surgery followed by radiation therapy. Surgery may be a lumpectomy or a mastectomy (e.g., total, simple or radical). Even if the doctor removes all of the cancer that can be seen at the time of surgery, the patient may be given radiation therapy, chemotherapy, or hormone therapy after surgery to try to kill any cancer cells that may be left. Radiation therapy is the use of x-rays or other types of radiation to kill cancer cells and shrink tumors. Radiation therapy may use external radiation (using a machine outside the body) or internal radiation. Chemotherapy is the use of drugs to kill cancer cells. Chemotherapy may be taken by mouth, or it may be put into the body by inserting a needle into a vein or muscle. Hormone therapy often focuses on estrogen and progesterone, which are hormones that affect the way some cancers grow. If tests show that the cancer cells have estrogen and progesterone receptors (molecules found in some cancer cells to which estrogen and progesterone will attach), hormone therapy is used to block the way these hormones help the cancer grow. Hormone therapy with tamoxifen is often given to patients with early stages of breast cancer and those with metastatic breast cancer. Other types of treatment being tested in clinical trials include sentinel lymph node biopsy followed by surgery and high-dose chemotherapy with bone marrow transplantation and peripheral blood stem cell transplantation. Any preventative/therapeutic treatment known in the art may be prescribed and/or administered, including, for example, surgery, chemotherapy and/or radiation treatment, and any of the treatments may be used

in combination with one another to treat or prevent breast cancer (e.g., surgery followed by radiation therapy).

[0222] Also provided are methods of preventing or treating cancer comprising providing an individual in need of such treatment with a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* inhibitor that reduces or inhibits the overexpression of mutant *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* (e.g., a *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* polynucleotide with an allele that is associated with cancer). Included herein are methods of reducing or blocking the expression of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* comprising providing or administering to individuals in need of reducing or blocking the expression of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* a pharmaceutical or physiologically acceptable composition comprising a molecule capable of inhibiting expression of *DLG1*, *KIAA0783*, *DPF3* or *CENPC1*, e.g., a siRNA molecule. Also included herein are methods of reducing or blocking the expression of secondary regulatory genes regulated by *DLG1*, *KIAA0783*, *DPF3* or *CENPC1* that play a role in oncogenesis which comprises introducing competitive inhibitors that target *DLG1*, *KIAA0783*, *DPF3* or *CENPC1*'s effect on these regulatory genes or that block the binding of positive factors necessary for the expression of these regulatory genes.

[0223] The examples set forth below are intended to illustrate but not limit the invention.

Examples

[0224] In the following studies a group of subjects were selected according to specific parameters relating to breast cancer. Nucleic acid samples obtained from individuals in the study group were subjected to genetic analysis, which identified associations between breast cancer and certain polymorphic regions in the *DLG1*, *KIAA0783*, *DPF3* and *CENPC1* genes (herein referred to as "target genes", "target nucleotides", "target polypeptides" or simply "targets"). Methods are described for producing *DLG1*, *KIAA0783*, *DPF3* and *CENPC1* polypeptides and polypeptide variants *in vitro* or *in vivo*. *DLG1*, *KIAA0783*, *DPF3* and *CENPC1* nucleic acids or polypeptides and variants thereof are utilized for screening test molecules for those that interact with *DLG1*, *KIAA0783*, *DPF3* and *CENPC1* molecules. Test molecules identified as interactors with *DLG1*, *KIAA0783*, *DPF3* and *CENPC1* molecules and variants are further screened *in vivo* to determine whether they treat breast cancer.

Example 1

Samples and Pooling Strategies

Sample Selection

[0225] Blood samples were collected from individuals diagnosed with breast cancer, which were referred to as case samples. Also, blood samples were collected from individuals not diagnosed with breast cancer as gender and age-matched controls. All of the samples were of German/German

descent. A database was created that listed all phenotypic trait information gathered from individuals for each case and control sample. Genomic DNA was extracted from each of the blood samples for genetic analyses.

DNA Extraction from Blood Samples

[0226] Six to ten milliliters of whole blood was transferred to a 50 ml tube containing 27 ml of red cell lysis solution (RCL). The tube was inverted until the contents were mixed. Each tube was incubated for 10 minutes at room temperature and inverted once during the incubation. The tubes were then centrifuged for 20 minutes at 3000 x g and the supernatant was carefully poured off. 100-200 µl of residual liquid was left in the tube and was pipetted repeatedly to resuspend the pellet in the residual supernatant. White cell lysis solution (WCL) was added to the tube and pipetted repeatedly until completely mixed. While no incubation was normally required, the solution was incubated at 37°C or room temperature if cell clumps were visible after mixing until the solution was homogeneous. 2 ml of protein precipitation was added to the cell lysate. The mixtures were vortexed vigorously at high speed for 20 sec to mix the protein precipitation solution uniformly with the cell lysate, and then centrifuged for 10 minutes at 3000 x g. The supernatant containing the DNA was then poured into a clean 15 ml tube, which contained 7 ml of 100% isopropanol. The samples were mixed by inverting the tubes gently until white threads of DNA were visible. Samples were centrifuged for 3 minutes at 2000 x g and the DNA was visible as a small white pellet. The supernatant was decanted and 5 ml of 70% ethanol was added to each tube. Each tube was inverted several times to wash the DNA pellet, and then centrifuged for 1 minute at 2000 x g. The ethanol was decanted and each tube was drained on clean absorbent paper. The DNA was dried in the tube by inversion for 10 minutes, and then 1000 µl of 1X TE was added. The size of each sample was estimated, and less TE buffer was added during the following DNA hydration step if the sample was smaller. The DNA was allowed to rehydrate overnight at room temperature, and DNA samples were stored at 2-8°C.

[0227] DNA was quantified by placing samples on a hematology mixer for at least 1 hour. DNA was serially diluted (typically 1:80, 1:160, 1:320, and 1:640 dilutions) so that it would be within the measurable range of standards. 125 µl of diluted DNA was transferred to a clear U-bottom microtitre plate, and 125 µl of 1X TE buffer was transferred into each well using a multichannel pipette. The DNA and 1X TE were mixed by repeated pipetting at least 15 times, and then the plates were sealed. 50 µl of diluted DNA was added to wells A5-H12 of a black flat bottom microtitre plate. Standards were inverted six times to mix them, and then 50 µl of 1X TE buffer was pipetted into well A1, 1000 ng/ml of standard was pipetted into well A2, 500 ng/ml of standard was pipetted into well A3, and 250 ng/ml of standard was pipetted into well A4. PicoGreen (Molecular Probes, Eugene, Oregon) was thawed and freshly diluted 1:200 according to the number of plates that were being measured.

PicoGreen was vortexed and then 50 μ l was pipetted into all wells of the black plate with the diluted DNA. DNA and PicoGreen were mixed by pipetting repeatedly at least 10 times with the multichannel pipette. The plate was placed into a Fluoroskan Ascent Machine (microplate fluorometer produced by Labsystems) and the samples were allowed to incubate for 3 minutes before the machine was run using filter pairs 485 nm excitation and 538 nm emission wavelengths. Samples having measured DNA concentrations of greater than 450 ng/ μ l were re-measured for conformation. Samples having measured DNA concentrations of 20 ng/ μ l or less were re-measured for confirmation.

Pooling Strategies

[0228] Samples were placed into one of two groups based on disease status. The two groups were female case groups and female control groups. A select set of samples from each group were utilized to generate pools, and one pool was created for each group. Each individual sample in a pool was represented by an equal amount of genomic DNA. For example, where 25 ng of genomic DNA was utilized in each PCR reaction and there were 200 individuals in each pool, each individual would provide 125 pg of genomic DNA. Inclusion or exclusion of samples for a pool was based upon the following criteria: the sample was derived from an individual characterized as Caucasian; the sample was derived from an individual of German paternal and maternal descent; the database included relevant phenotype information for the individual; case samples were derived from individuals diagnosed with breast cancer; control samples were derived from individuals free of cancer and no family history of breast cancer; and sufficient genomic DNA was extracted from each blood sample for all allelotyping and genotyping reactions performed during the study. Phenotype information included pre- or post-menopausal, familial predisposition, country or origin of mother and father, diagnosis with breast cancer (date of primary diagnosis, age of individual as of primary diagnosis, grade or stage of development, occurrence of metastases, e.g., lymph node metastases, organ metastases), condition of body tissue (skin tissue, breast tissue, ovary tissue, peritoneum tissue and myometrium), method of treatment (surgery, chemotherapy, hormone therapy, radiation therapy). Samples that met these criteria were added to appropriate pools based on gender and disease status.

[0229] The selection process yielded the pools set forth in Table 1, which were used in the studies that follow:

Table 1

	Female CASE	Female CONTROL
Pool size (Number)	272	276
Pool Criteria (ex: case/control)	case	control

Mean Age (ex: years)	59.6	55.4
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Example 2

Association of Polymorphic Variants with Breast cancer

[0230] A whole-genome screen was performed to identify particular SNPs associated with occurrence of breast cancer. As described in Example 1, two sets of samples were utilized, which included samples from female individuals having breast cancer (breast cancer cases) and samples from female individuals not having cancer (female controls). The initial screen of each pool was performed in an allelotyping study, in which certain samples in each group were pooled. By pooling DNA from each group, an allele frequency for each SNP in each group was calculated. These allele frequencies were then compared to one another. Particular SNPs were considered as being associated with breast cancer when allele frequency differences calculated between case and control pools were statistically significant. SNP disease association results obtained from the allelotyping study were then validated by genotyping each associated SNP across all samples from each pool. The results of the genotyping were then analyzed, allele frequencies for each group were calculated from the individual genotyping results, and a p-value was calculated to determine whether the case and control groups had statistically significant differences in allele frequencies for a particular SNP. When the genotyping results agreed with the original allelotyping results, the SNP disease association was considered validated at the genetic level.

SNP Panel Used for Genetic Analyses

[0231] A whole-genome SNP screen began with an initial screen of approximately 25,000 SNPs over each set of disease and control samples using a pooling approach. The pools studied in the screen are described in Example 1. The SNPs analyzed in this study were part of a set of 25,488 SNPs confirmed as being statistically polymorphic as each is characterized as having a minor allele frequency of greater than 10%. The SNPs in the set reside in genes or in close proximity to genes, and many reside in gene exons. Specifically, SNPs in the set are located in exons, introns, and within 5,000 base-pairs upstream of a transcription start site of a gene. In addition, SNPs were selected according to the following criteria: they are located in ESTs; they are located in Locuslink or Ensemble genes; and they are located in Genomatix promoter predictions. SNPs in the set also were selected on the basis of even spacing across the genome, as depicted in Table 2.

[0232] A case-control study design using a whole genome association strategy involving approximately 28,000 single nucleotide polymorphisms (SNPs) was employed. Approximately 25,000 SNPs were evenly spaced in gene-based regions of the human genome with a median inter-marker distance of about 40,000 base pairs. Additionally, approximately 3,000 SNPs causing amino acid substitutions in genes described in the literature as candidates for various diseases were used. The

case-control study samples were of female German origin (German paternal and maternal descent) 548 individuals were equally distributed in two groups (female controls and female cases). The whole genome association approach was first conducted on 2 DNA pools representing the 2 groups. Significant markers were confirmed by individual genotyping.

Table 2

General Statistics		Spacing Statistics	
Total # of SNPs	25,488	Median	37,058 bp
# of Exonic SNPs	>4,335 (17%)	Minimum*	1,000 bp
# SNPs with refSNP ID	20,776 (81%)	Maximum*	3,000,000 bp
Gene Coverage	>10,000	Mean	122,412 bp
Chromosome Coverage	All	Std Deviation	373,325 bp
		*Excludes outliers	

Allelotyping and Genotyping Results

[0233] The genetic studies summarized above and described in more detail below identified allelic variants associated with breast cancer. The allelic variants identified from the SNP panel described in Table 2 are summarized below in Table 3.

Table 3

SNP Reference	Chromosome Position	Position in Figs 1-4	Contig Identification	Contig Position	Sequence Identification	Sequence Position	Allelic Variability
rs1949471	198272877	39977	NT_029928	1484976	NM_004087	Exonic (R278Q)	T/C
rs220097	10793860	49860	NT_007819	10345196	NM_014660	intragenic	T/C
rs1990440	71267195	40095	NT_026437	53197195	NM_012074	intragenic	G/C
rs355510	68321769	46769	NT_022778	8587277	NM_001812	intragenic	G/A

[0234] Table 3 includes information pertaining to the incident polymorphic variant associated with breast cancer identified herein. Public information pertaining to the polymorphism and the genomic sequence that includes the polymorphism are indicated. The genomic sequences identified in Table 3 may be accessed at the [http address www.ncbi.nih.gov/entrez/query.fcgi](http://www.ncbi.nih.gov/entrez/query.fcgi), for example, by using the publicly available SNP reference number (e.g., rs1949471). The chromosome position refers to the position of the SNP within NCBI's Genome Build 33, which may be accessed at the following [http address: www.ncbi.nlm.nih.gov/mapview/map_search.cgi?chr=hum_chr.inf&query=](http://www.ncbi.nlm.nih.gov/mapview/map_search.cgi?chr=hum_chr.inf&query=). The "Contig Position" provided in Table 3 corresponds to a nucleotide position set forth in the contig sequence, and designates the polymorphic site corresponding to the SNP reference number. The sequence containing the polymorphisms also may be referenced by the "Sequence Identification" set forth in Table 3. The "Sequence Identification" corresponds to cDNA sequence that encodes associated target polypeptides (e.g., *DLG1*) of the invention. The position of the SNP within the

cDNA sequence is provided in the "Sequence Position" column of Table 3. Also, the allelic variation at the polymorphic site and the allelic variant identified as associated with breast cancer is specified in Table 3. All nucleotide sequences referenced and accessed by the parameters set forth in Table 3 are incorporated herein by reference. rs220097 also is known rs286246.

Assay for Verifying, Allelotyping, and Genotyping SNPs

[0235] A MassARRAY™ system (Sequenom, Inc.) was utilized to perform SNP genotyping in a high-throughput fashion. This genotyping platform was complemented by a homogeneous, single-tube assay method (hME™ or homogeneous MassEXTEND™ (Sequenom, Inc.)) in which two genotyping primers anneal to and amplify a genomic target surrounding a polymorphic site of interest. A third primer (the MassEXTEND™ primer), which is complementary to the amplified target up to but not including the polymorphism, was then enzymatically extended one or a few bases through the polymorphic site and then terminated.

[0236] For each polymorphism, SpectroDESIGNER™ software (Sequenom, Inc.) was used to generate a set of PCR primers and a MassEXTEND™ primer was used to genotype the polymorphism. Table 4 shows PCR primers and Table 5 shows extension primers used for analyzing polymorphisms. The initial PCR amplification reaction was performed in a 5 µl total volume containing 1X PCR buffer with 1.5 mM MgCl₂ (Qiagen), 200 µM each of dATP, dGTP, dCTP, dTTP (Gibco-BRL), 2.5 ng of genomic DNA, 0.1 units of HotStar DNA polymerase (Qiagen), and 200 nM each of forward and reverse PCR primers specific for the polymorphic region of interest.

Table 4: PCR Primers

Reference SNP ID	Forward PCR primer	Reverse PCR primer
rs1949471	ACGTTGGATGGCTTCAACTGCTTTGCTA TG	ACGTTGGATGTTTCTCAGGGTCAATGACT G
rs220097	GCAACGTCACATTTCAC	TTCTGGGAATGGATTTCAG
rs1990440	CCAGGGTGTGTTCTAATACG	AAGTCACTAACCCACACAC
rs355510	TTCTGAGATGATCCTGATGG	CCCTCCTTTTAACCTTTTAGG

[0237] Samples were incubated at 95°C for 15 minutes, followed by 45 cycles of 95°C for 20 seconds, 56°C for 30 seconds, and 72°C for 1 minute, finishing with a 3 minute final extension at 72°C. Following amplification, shrimp alkaline phosphatase (SAP) (0.3 units in a 2 µl volume) (Amersham Pharmacia) was added to each reaction (total reaction volume was 7 µl) to remove any residual dNTPs that were not consumed in the PCR step. Samples were incubated for 20 minutes at 37°C, followed by 5 minutes at 85°C to denature the SAP.

[0238] Once the SAP reaction was complete, a primer extension reaction was initiated by adding a polymorphism-specific MassEXTEND™ primer cocktail to each sample. Each MassEXTEND™

cocktail included a specific combination of dideoxynucleotides (ddNTPs) and deoxynucleotides (dNTPs) used to distinguish polymorphic alleles from one another. In Table 5, ddNTPs are shown and the fourth nucleotide not shown is the dNTP.

Table 5: Extend Primers

Reference SNP ID	Extend Probe	Term Mix
rs1949471	CAGGGTCAATGACTGTATATTAC	ACT
rs220097	ACAGAGTTTTAAACCTCCTACA	ACT
rs1990440	CGTCAGCAAATGTGTACCGA	ACT
rs355510	ATGGTTTTCTTTCTTGTCTTC	ACG

[0239] The MassEXTEND™ reaction was performed in a total volume of 9 µl, with the addition of 1X ThermoSequenase buffer, 0.576 units of ThermoSequenase (Amersham Pharmacia), 600 nM MassEXTEND™ primer, 2 mM of ddATP and/or ddCTP and/or ddGTP and/or ddTTP, and 2 mM of dATP or dCTP or dGTP or dTTP. The deoxy nucleotide (dNTP) used in the assay normally was complementary to the nucleotide at the polymorphic site in the amplicon. Samples were incubated at 94°C for 2 minutes, followed by 55 cycles of 5 seconds at 94°C, 5 seconds at 52°C, and 5 seconds at 72°C.

[0240] Following incubation, samples were desalted by adding 16 µl of water (total reaction volume was 25 µl), 3 mg of SpectroCLEAN™ sample cleaning beads (Sequenom, Inc.) and allowed to incubate for 3 minutes with rotation. Samples were then robotically dispensed using a piezoelectric dispensing device (SpectroJET™ (Sequenom, Inc.)) onto either 96-spot or 384-spot silicon chips containing a matrix that crystallized each sample (SpectroCHIP® (Sequenom, Inc.)). Subsequently, MALDI-TOF mass spectrometry (Biflex and Autoflex MALDI-TOF mass spectrometers (Bruker Daltonics) can be used) and SpectroTYPER RT™ software (Sequenom, Inc.) were used to analyze and interpret the SNP genotype for each sample.

Genetic Analysis

[0241] Variations identified in the target genes are provided in their respective genomic sequences (see Figures 1-5) Minor allelic frequencies for these polymorphisms was verified as being 10% or greater by determining the allelic frequencies using the extension assay described above in a group of samples isolated from 92 individuals originating from the state of Utah in the United States, Venezuela and France (Coriell cell repositories).

[0242] Genotyping results are shown for female pools in Table 6A and 6B. Table 6A shows the original genotyping results and Table 6B shows the genotyped results re-analyzed to remove duplicate individuals from the cases and controls (*i.e.*, individuals who were erroneously included more than

once as either cases or controls). Therefore, Table 6B represents a more accurate measure of the allele frequencies for this particular SNP. In the subsequent tables, "AF" refers to allelic frequency; and "F case" and "F control" refer to female case and female control groups, respectively.

Table 6A

Reference SNP ID	AF F case	AF F control	p-value	Odds Ratio	Breast Cancer Assoc. Allele
rs1949471	T = 0.186 C = 0.814	T = 0.112 C = 0.890	0.0005	0.54	T
rs220097	T = 0.721 C = 0.279	T = 0.626 C = 0.374	0.0014	0.66	T
rs1990440	C = 0.876 G = 0.124	C = 0.926 G = 0.074	0.0027	0.65	G
rs355510	A = 0.545 G = 0.455	A = 0.616 G = 0.384	0.0173	0.75	G

Table 6B

Reference SNP ID	AF F case	AF F control	p-value	Odds Ratio	Breast Cancer Assoc. Allele
rs1949471	T = 0.182 C = 0.818	T = 0.108 C = 0.892	0.0009	0.54	T
rs220097	T = 0.709 C = 0.291	T = 0.624 C = 0.376	0.0045	0.68	T
rs1990440	C = 0.879 G = 0.121	C = 0.915 G = 0.085	0.0692	0.67	G
rs355510	A = 0.539 G = 0.461	A = 0.617 G = 0.383	0.0123	0.73	G

[0243] The single marker alleles set forth in Table 3 were considered validated, since the genotyping data for the females, males or both pools were significantly associated with breast cancer, and because the genotyping results agreed with the original allelotyping results. Particularly significant associations with breast cancer are indicated by a calculated p-value of less than 0.05 for genotype results, which are set forth in bold text. Tables 6A and 6B show the disease associated allele in column 6. In the case of rs1949471, this SNP is an exonic SNP that codes for a R278Q amino acid change in the DLG1 gene. The thymine allele codes for glutamine (Q); therefore, a glutamine is associated with an increased risk of breast cancer.

[0244] Odds ratio results are shown in Tables 6A and 6B. An odds ratio is an unbiased estimate of relative risk which can be obtained from most case-control studies. Relative risk (RR) is an estimate of the likelihood of disease in the exposed group (susceptibility allele or genotype carriers) compared to the unexposed group (not carriers). It can be calculated by the following equation:

$$RR = IA/Ia$$

IA is the incidence of disease in the A carriers and Ia is the incidence of disease in the non-carriers.

$RR > 1$ indicates the A allele increases disease susceptibility.

$RR < 1$ indicates the a allele increases disease susceptibility.

[0245] For example, $RR = 1.5$ indicates that carriers of the A allele have 1.5 times the risk of disease than non-carriers, *i.e.*, 50% more likely to get the disease.

[0246] Case-control studies do not allow the direct estimation of IA and Ia , therefore relative risk cannot be directly estimated. However, the odds ratio (OR) can be calculated using the following equation:

$$OR = (nDA nDa) / (nA nDa) = pDA(1 - pDA) / pA(1 - pDA), \text{ or}$$

$OR = ((\text{case } f) / (1 - \text{case } f)) / ((\text{control } f) / (1 - \text{control } f))$, where f = susceptibility allele frequency.

[0247] An odds ratio can be interpreted in the same way a relative risk is interpreted and can be directly estimated using the data from case-control studies, *i.e.*, case and control allele frequencies. The higher the odds ratio value, the larger the effect that particular allele has on the development of breast cancer. Possessing an allele associated with a relatively high odds ratio translates to having a higher risk of developing or having breast cancer.

Example 3

DLG1 Region Proximal SNPs

[0248] It has been discovered that a polymorphic variation (rs1949471) in a region that encodes the discs, large homolog 1 (Drosophila) (DLG1) gene is associated with the occurrence of breast cancer (see Examples 1 and 2). Subsequently, SNPs proximal to the incident SNP (rs1949471) were identified and allelotyped in breast cancer sample sets and control sample sets as described in Examples 1 and 2. Approximately twenty-one allelic variants located within the DLG1 region were identified and allelotyped. The polymorphic variants are set forth in Table 7. The chromosome position provided in column four of Table 7 is based on Genome "Build 33" of NCBI's GenBank.

Table 7

dbSNP rs#	Chromosome	Chromosome Position	Position in Figure 1	Allele Variants
2341225	3	198233033	133	T/C
3856760	3	198240838	7938	T/C
2195027	3	198241773	8873	G/A
1356612	3	198246121	13221	C/T
3773845	3	198250188	17288	T/C
2098941	3	198258632	25732	G/A
890491	3	198259823	26923	C/G
1949471	3	198272877	39977	C/T

dbSNP rs#	Chromosome	Chromosome Position	Position in Figure 1	Allele Variants
3773851	3	198274184	41284	T/A
3773852	3	198274310	41410	A/C
3773853	3	198274377	41477	C/T
1195059	3	198274414	41514	G/A
3773855	3	198275506	42606	G/A
3821713	3	198275642	42742	A/C
604005	3	198292415	59515	G/A
DLG1 SNP	3	198292708	59808	T/C
2879969	3	198293165	60265	C/G
958902	3	198300052	67152	T/C
1839742	3	198301232	68332	T/C
1868890	3	198304028	71128	T/C
1868891	3	198309327	76427	G/A

Assay for Verifying and Allelotyping SNPs

[0249] The methods used to verify and allelotype the proximal SNPs of Table 7 are the same methods described in Examples 1 and 2 herein. The PCR primers and extend primers used in these assays are provided in Table 8 and Table 9, respectively.

Table 8

dbSNP rs#	Forward PCR primer	Reverse PCR primer
604005	ACGTTGGATGTGTCTCGCTTTTAGCCTGTG	ACGTTGGATGCAGACAGACATACAGAAGGG
890491	ACGTTGGATGGCAGAACCATGGAGAAAAGC	ACGTTGGATGGGCAAGAGTAAGGCACTATC
958902	ACGTTGGATGGCCACTGAATTGTACATTAAC	ACGTTGGATGATTGGAGTCCCGAGCTAAAC
1195059	ACGTTGGATGCCTGTTTTCATTTAGACTCC	ACGTTGGATGTGCTCACAAAGATTAAACC
1356612	ACGTTGGATGTTGAACAGCTCAGCTGAAAG	ACGTTGGATGAGATACATGTCTTGTCTGGG
1839742	ACGTTGGATGTCTGAGGTCAGGAGTTTGAG	ACGTTGGATGGCCACCATGTCCAGCTAATT
1868890	ACGTTGGATGAGTGAGGAAGGCCTATTAAC	ACGTTGGATGATACCTGAGTCGAACCTTTG
1868891	ACGTTGGATGTTATTGCTCTTGAACGTGGC	ACGTTGGATGTCTGAGAAAAAGAAATTGGGG
1949471	ACGTTGGATGTTTCTCAGGGTCAATGACTG	ACGTTGGATGAGACCTGCTTCTTTCAACG
2098941	ACGTTGGATGATTAGCTGGGCATGCTATCC	ACGTTGGATGTGTAGCCTTGAATTCCTGGG
2195027	ACGTTGGATGGGCGCTAAATAATGCGCCAC	ACGTTGGATGCTGACCTCGTGATCTGCCTG
2341225	ACGTTGGATGGGCGGGTGGGAAGACTCTAA	ACGTTGGATGTCTTTCAGTGTATTTCAGATC
2879969	ACGTTGGATGCTCCATTTCAAAAAAAAAAAAA	ACGTTGGATGCCTTAGAGGTATGTCCAGAG
3773845	ACGTTGGATGACACAAGTAACAAACTTGAG	ACGTTGGATGGTGCTTGAAGAAATTATGTG
3773851	ACGTTGGATGTAAGATACGGAGGATAGAGG	ACGTTGGATGGCATATAGTCTTTGTGGTGTG
3773852	ACGTTGGATGGTGAGTGTACTTAAATAAGTT	ACGTTGGATGGTTTCCCTTTGTGTTTTCAG
3773853	ACGTTGGATGTGGTTTAAATCTTTGTGAGC	ACGTTGGATGCTGTGAGTGTATCTGAAAAC
3773855	ACGTTGGATGGCTTGTTTATGAAGTGGAG	ACGTTGGATGTTAATACCATTGGTTAAATC
3821713	ACGTTGGATGTTCAAGCAACTCAAGTAAGC	ACGTTGGATGTAGAGTGGGTGTTTACACTG
3856760	ACGTTGGATGTGATCTCAGCTCACTGTAAC	ACGTTGGATGTGTAGTCCAGCTACTCAGG
FCH-1723	ACGTTGGATGGCTTCAACTGCTTTGCTATG	ACGTTGGATGTTTCTCAGGGTCAATGACTG
DLG1 SNP	ACGTTGGATGCTTCATAGTAGCCAGGCTAG	ACGTTGGATGAGCACATGAACAGATGTGTC

Table 9

dbSNP rs#	Extend Primer	Term Mix
604005	TTATCAACCTACAATGGA	ACG
890491	TTATGGCCATACGTAAAAAGCA	ACT
958902	CGGAGGCTTTATTTCGTA	ACT
1195059	AAAGATTTAAACCATCAACCAAAT	ACG
1356612	GGGTAGTGGTTTCATGATTTTTA	ACG
1839742	TCCAGCTAATTTTTGTATTTTTA	ACT
1868890	CTGAGTCGAACTCTTGATAAA	ACT
1868891	GAAAAAGAATTGGGGATTATAAC	ACG
1949471	CGAACATCTACTTCATTTACT	ACG
2098941	TCCTCCACATCAGCCT	ACG
2195027	GCGTGAGCCACCACACC	ACG
2341225	CACTGTATTCAGATCTTCATATTT	ACT
2879969	CATCATACTGCCTCTGG	ACT
3773845	TTATGTGTTCTCTATTTATTGACT	ACT
3773851	TTTGTGGTGTGGGATTC	CGT
3773852	TATTTTCCATTTCTCTCTG	ACT
3773853	AAGGGAACTCATGATTTCTA	ACG
3773855	AGGCTTTTTGTAGCAGT	ACG
3821713	GTGGGTGTTTACACTGTTTAATAC	ACT
3856760	ATGAGAATCACTTGAACCTG	ACT
FCH-1723	CAGGGTCAATGACTGTATATTAC	ACT
DLG1 SNP	AGATGTGTCACAAATGCAA	ACT

Genetic Analysis of Allelotyping Results

[0250] Allelotyping results are shown for cases and controls in Table 10. The allele frequency for the A2 allele is noted in the fifth and sixth columns for breast cancer pools and control pools, respectively, where “AF” is allele frequency. The allele frequency for the A1 allele can be easily calculated by subtracting the A2 allele frequency from 1 ($A1\ AF = 1 - A2\ AF$). For example, the SNP rs2341225 has the following case and control allele frequencies: case A1 (T) = 0.747; case A2 (C) = 0.253; control A1 (T) = 0.743; and control A2 (C) = 0.257, where the nucleotide is provided in paranthesis. SNPs with blank allele frequencies were untyped.

Table 10

dbSNP rs#	Chromosome	Position in Figure 1	Allele Variants	A2 Case AF	A2 Control AF	p-Value
2341225	198233033	133	T/C	0.253	0.257	0.8897
3856760	198240838	7938	T/C	0.959	0.985	0.0095
2195027	198241773	8873	G/A	0.651	0.691	0.1538
1356612	198246121	13221	C/T	0.197	0.243	0.0653
3773845	198250188	17288	T/C	0.415	0.414	0.9646
2098941	198258632	25732	G/A	0.281	0.335	0.0515
890491	198259823	26923	C/G	0.440	0.525	0.0051

dbSNP rs#	Chromosome	Position in Figure 1	Allele Variants	A2 Case AF	A2 Control AF	p-Value
1949471	198272877	39977	C/T	0.181	0.092	0.0001
3773851	198274184	41284	T/A	0.351	0.371	0.4824
3773852	198274310	41410	A/C	0.206	0.233	0.2786
3773853	198274377	41477	C/T	0.485	0.480	0.8660
1195059	198274414	41514	G/A	0.936	0.931	0.7361
3773855	198275506	42606	G/A	0.275	0.260	0.5723
3821713	198275642	42742	A/C	0.728	0.677	0.0666
604005	198292415	59515	G/A	0.985	0.986	0.8647
DLG1 SNP	198292708	59808	T/C	0.723	0.825	0.0002
2879969	198293165	60265	C/G	0.589	0.596	0.8093
958902	198300052	67152	T/C	0.215	0.264	0.0568
1839742	198301232	68332	T/C	0.928	0.946	0.2311
1868890	198304028	71128	T/C	0.420	0.422	0.9494
1868891	198309327	76427	G/A	0.220	0.217	0.8858

[0251] Figure 13 shows the proximal SNPs in and around the DLG1 gene. The position of each SNP on the chromosome is presented on the x-axis. The y-axis gives the negative logarithm (base 10) of the p-value comparing the estimated allele in the case group to that of the control group. The minor allele frequency of the control group for each SNP designated by an X or other symbol on the graphs in Figure 13 can be determined by consulting Table 10. By proceeding down the Table from top to bottom and across the graphs from left to right the allele frequency associated with each symbol shown can be determined.

[0252] To aid the interpretation, multiple lines have been added to the graph. The broken horizontal lines are drawn at two common significance levels, 0.05 and 0.01. The vertical broken lines are drawn every 20kb to assist in the interpretation of distances between SNPs. Two other lines are drawn to expose linear trends in the association of SNPs to the disease. The light gray line (or generally bottom-most curve) is a nonlinear smoother through the data points on the graph using a local polynomial regression method (W.S. Cleveland, E. Grosse and W.M. Shyu (1992) Local regression models. Chapter 8 of Statistical Models in S eds J.M. Chambers and T.J. Hastie, Wadsworth & Brooks/Cole.). The black line (or generally top-most curve, *e.g.*, see peak in left-most graph just to the left of position 92150000) provides a local test for excess statistical significance to identify regions of association. This was created by use of a 10kb sliding window with 1kb step sizes. Within each window, a chi-square goodness of fit test was applied to compare the proportion of SNPs that were significant at a test wise level of 0.01, to the proportion that would be expected by chance alone (0.05 for the methods used here). Resulting p-values that were less than 10^{-8} were truncated at that value.

[0253] Finally, the gene or genes present in the loci region of the proximal SNPs as annotated by Locus Link ([http address: www.ncbi.nlm.nih.gov/LocusLink/](http://www.ncbi.nlm.nih.gov/LocusLink/)) are provided on the graph. The exons and introns of the genes in the covered region are plotted below each graph at the appropriate chromosomal positions. The gene boundary is indicated by the broken horizontal line. The exon

positions are shown as thick, unbroken bars. An arrow is placed at the 3' end of each gene to show the direction of transcription.

Example 4

KIAA0783 Proximal SNPs

[0254] It has been discovered that a polymorphic variation (rs220097) in a region that encodes KIAA0783 is associated with the occurrence of breast cancer (see Examples 1 and 2). Subsequently, SNPs proximal to the incident SNP (rs220097) were identified and allelotyped in breast cancer sample sets and control sample sets as described in Examples 1 and 2. Approximately fifty-eight allelic variants located within the KIAA0783 region were identified and allelotyped. The polymorphic variants are set forth in Table 11.

Table 11

dbSNP rs#	Chromosome	Position in Figure 2	Chromosome Position	Allele Variants
218973	7	201	10710201	G/A
218962	7	6395	10716395	T/C
1640705	7	8558	10718558	T/C
218983	7	9429	10719429	C/T
190075	7	9809	10719809	T/G
284856	7	10072	10720072	C/T
218981	7	10511	10720511	C/T
218980	7	11556	10721556	C/G
1640703	7	16857	10726857	A/G
1640702	7	16951	10726951	A/G
1640701	7	17027	10727027	C/G
1681305	7	17177	10727177	T/C
1640700	7	17615	10727615	A/C
1640699	7	17950	10727950	C/G
1154923	7	18329	10728329	T/G
1154922	7	18384	10728384	T/C
1154921	7	18561	10728561	G/A
1154920	7	18579	10728579	C/T
2510348	7	18871	10728871	C/G
1681311	7	27152	10737152	C/T
1681312	7	27306	10737306	T/C
1681286	7	28091	10738091	T/C
1640710	7	28661	10738661	A/C
1681284	7	29011	10739011	T/C
2110377	7	29962	10739962	T/G
2110376	7	29969	10739969	T/G
2160059	7	30085	10740085	T/C
1681290	7	31656	10741656	A/G
1681291	7	31685	10741685	A/G
1681292	7	31749	10741749	G/A
220091	7	45389	10755389	T/C
182594	7	45459	10755459	G/C
220090	7	46647	10756647	A/G

dbSNP rs#	Chromosome	Position in Figure 2	Chromosome Position	Allele Variants
220097	7	49860	10759860	T/C
220096	7	53061	10763061	T/C
220095	7	57308	10767308	T/A
3801435	7	61563	10771563	A/G
1681281	7	61660	10771660	A/G
1026903	7	62212	10772212	C/T
220093	7	67090	10777090	T/G
286243	7	67198	10777198	T/C
3801437	7	70071	10780071	A/G
3801438	7	70191	10780191	G/A
2108111	7	74006	10784006	C/T
2353340	7	75600	10785600	A/G
3823875	7	85761	10795761	A/G
2190295	7	90798	10800798	T/G
KIAA0783_SNP1	7	90883	10800883	C/T
2306768	7	91259	10801259	T/A
2353341	7	95416	10805416	C/G
2353342	7	95446	10805446	T/G
2883140	7	96368	10806368	G/T
2353343	7	97050	10807050	T/C
2108114	7	97362	10807362	C/T
1483204	7	97630	10807630	A/C
1483202	7	97989	10807989	T/C
1483201	7	98107	10808107	C/T
KIAA0783_SNP2	7	NOT MAPPED		

Assay for Verifying and Allelotyping SNPs

[0255] The methods used to verify and allelotype the proximal SNPs of Table 11 are the same methods described in Examples 1 and 2 herein. The PCR primers and extend primers used in these assays are provided in Table 12 and Table 13, respectively.

Table 12

dbSNP rs#	Forward PCR primer	Reverse PCR primer
KIAA0783_SNP1	ACGTTGGATGCCCTAACACTACTCCTTGTC	ACGTTGGATGCCAACACTTCTTGGAGTCTG
KIAA0783_SNP2	ACGTTGGATGAGCCACATTCTCAGATACTG	ACGTTGGATGGGAAAAGAAGGAAGAAGAAG
182594	ACGTTGGATGGAGACAGAAAAGTGGTGGAC	ACGTTGGATGCCTTTAAGAAGGCCCTTGTG
190075	ACGTTGGATGCACAAATTCAGTGGCCAAGC	ACGTTGGATGCTTGTGTGGACACCTACTG
218962	ACGTTGGATGCAGGAGTGAGAAGTTCTTTG	ACGTTGGATGTGCTGATTGGTCTATGGGTG
218973	ACGTTGGATGTCTCACACTGAGGCCTGTAG	ACGTTGGATGTTTGCTGCACCCATCAACTC
218980	ACGTTGGATGCTTCCCTCCTTTTCTCCTTC	ACGTTGGATGCAAGATCCAATCCAGAAGAC
218981	ACGTTGGATGAGATTGCTGCCACTACACAC	ACGTTGGATGCTCTTGGCATTCTTAACTCAG
218983	ACGTTGGATGTCTGCAGTTTCTCTCTCAAC	ACGTTGGATGACCAAATCCAAGATGTAGGG
220090	ACGTTGGATGCAGCAGAACTTGATGATGG	ACGTTGGATGAGACACTGAGACTCTGGAGG

dbSNP rs#	Forward PCR primer	Reverse PCR primer
220091	ACGTTGGATGGTGTATACACAAGGGCCTTC	ACGTTGGATGCTGATTGCTGTTTCTGTTAC
220093	ACGTTGGATGTCCACACTGTGAACAGAGAC	ACGTTGGATGAGTCTAAAAAGGCTGTCAGG
220095	ACGTTGGATGGCAGCTCAATTTTAGGAACC	ACGTTGGATGCCCTTGACACTGTTGCATG
220096	ACGTTGGATGTAGATTAATTATTGTTGGC	ACGTTGGATGGCCACCTCCAAAATTAGATC
220097	ACGTTGGATGTTCTCTGGGAATGGATTTGAG	ACGTTGGATGGCAAACGTGCACATTTGCAC
284856	ACGTTGGATGTGCATGACTACACAAAGAAG	ACGTTGGATGGCAAATCCTACATTGAGGC
286243	ACGTTGGATGATGTCTCTGTTACAGTGTG	ACGTTGGATGCTGGCAAATAGCAATCTAAAC
220097	ACGTTGGATGTTCTCTGGGAATGGATTTGAG	ACGTTGGATGGCAAACGTGCACATTTGCAC
1026903	ACGTTGGATGGTACTGAAACTCTGAGCATTG	ACGTTGGATGCATCTTATCTGTTTACCATAC
1154920	ACGTTGGATGGCTGTATATACGAGTTAATGG	ACGTTGGATGAGTGGAGGTGGAGGTGAGGCT
1154921	ACGTTGGATGAAATGCCAATAGCGCCAAGG	ACGTTGGATGAGTAGAAGAGATAAGCCTGG
1154922	ACGTTGGATGTTTTGCCCTACCAAGATTGC	ACGTTGGATGACAATTTTATTGAGGAGAGG
1154923	ACGTTGGATGGATGGTTGATCACTTGTGTAG	ACGTTGGATGCTTACCTCCTCTCCTCAATG
1483201	ACGTTGGATGGTTGCTAAAGTAGTTTCAGCC	ACGTTGGATGACCAAAGAGCTTGTCCCATC
1483202	ACGTTGGATGGTGCTTTAGAATGTAACACAG	ACGTTGGATGTGGAATTGCACCCTTGCTTG
1483204	ACGTTGGATGTATCTTATCTAGCAGGCAAC	ACGTTGGATGACTAAGATCACAGGCCTGAG
1640699	ACGTTGGATGGGTTGGGTGTATGATAGGAG	ACGTTGGATGAGCATGGCTAATCTGTCTGG
1640700	ACGTTGGATGCTTTATTGACTGCTTCAATC	ACGTTGGATGAGTGATTACGAGCCTGTACC
1640701	ACGTTGGATGTTAGGTGCATTGATGCTCTG	ACGTTGGATGCTCAGGCACAGAAAAGATTC
1640702	ACGTTGGATGCTGTGGTCTCAGGTCACAAA	ACGTTGGATGATGCACCTAAAACAAGAGTC
1640703	ACGTTGGATGCATAATTTACCTTCCTGGCC	ACGTTGGATGCAAATTTGTGACCTGAGACC
1640705	ACGTTGGATGACCATCAGAACCAGTATACC	ACGTTGGATGGATGGCCAGAATTGATGTAC
1640710	ACGTTGGATGCCTTTCCGCTGTATCTCTTG	ACGTTGGATGGGTACAAGGAAGATCCTCAG
1681281	ACGTTGGATGATTGAGAAAGCAGCTGCTTG	ACGTTGGATGCCAACCTCCCAAATACATCC
1681284	ACGTTGGATGATAAAATAGGTCTGGGGCTG	ACGTTGGATGGTTTGCTTACTCTGGTACTG
1681286	ACGTTGGATGGAATGTAACGCAAAGAGGG	ACGTTGGATGGTTGAAACATTGTCTGCTAG
1681290	ACGTTGGATGGTACCATAAAATACAATACC	ACGTTGGATGTGGTCCCCCAGTCATCTTAA
1681291	ACGTTGGATGTAGCAAAACCCTGCCTCTAC	ACGTTGGATGAGGTCAGTGTTCTGGTATTG
1681292	ACGTTGGATGAGGTCAGTGTTCTGGTATTG	ACGTTGGATGAGCCTGGGCAACATAGCAAA
1681305	ACGTTGGATGCAGACAGATGTTTAGCTACC	ACGTTGGATGTGAAGTTGTGGATTCCAGC
1681311	ACGTTGGATGGCTTGACCAATCATACTTCC	ACGTTGGATGGAAACAAATTGCTCTGAGTCC
1681312	ACGTTGGATGTCTTCAGGGCAGTAGGATTG	ACGTTGGATGCACATGTGTTTAATACAAGG
2108111	ACGTTGGATGAGCCTGTAAATGATAGAGCC	ACGTTGGATGGATGTCACAGTACAGCAATG
2108114	ACGTTGGATGGATAGAAAAGTTAGAGAAATG	ACGTTGGATGAAGGTCACACCACTGCACTC
2110376	ACGTTGGATGCCAGTTTACACTGGATATTTG	ACGTTGGATGTTGACTAGCTGCTAGAAGGG
2110377	ACGTTGGATGCCAGTTTACACTGGATATTTG	ACGTTGGATGTTGACTAGCTGCTAGAAGGG
2160059	ACGTTGGATGTTAAGTACCGGGAAATTGAG	ACGTTGGATGTCATATACCTACGCAGGCTC
2190295	ACGTTGGATGCTTTTAGAAGTAGTAGGGG	ACGTTGGATGAGACTCCAAGAAGTGTTGGG
2306768	ACGTTGGATGAAAGGTGGTTTTGCCAGCTG	ACGTTGGATGCTCAGTCTCCTGAAGTGCTG
2353340	ACGTTGGATGCCTATCTGCATGTTGCTTAC	ACGTTGGATGGACTCTTGGGAGTACAAATG
2353341	ACGTTGGATGCACAACCAGAAATTTGTAAGTC	ACGTTGGATGCACACGCATGCATCATCTAC
2353342	ACGTTGGATGTGGTTTTAGTCAAAGCTGC	ACGTTGGATGCTGAGATCTTCTTCCCTGAC
2353343	ACGTTGGATGGTTGCAGAGGGAAGCATTTG	ACGTTGGATGCACTTGTGACCAGGTCACCTA
2510348	ACGTTGGATGCTATCCCAGGGCTATGTTTG	ACGTTGGATGGAAGTGAGGATGAGTTGTG
2883140	ACGTTGGATGCAGCACTTACTTGTGATGTAG	ACGTTGGATGCATAACCAATTTGTCTTAAC
3801435	ACGTTGGATGTCAGTATGAAGCAAGCAGCC	ACGTTGGATGATGTCGCTATACTCTGTAGG
3801437	ACGTTGGATGGTAGCTGAGAAGATGCTCAC	ACGTTGGATGATAGCTGTTCCAGTCTCTTG
3801438	ACGTTGGATGATACGGTAAAGGTAGTCTGG	ACGTTGGATGTTACCTGTATTGCCCTCTCG
3823875	ACGTTGGATGCTCAAGAGCCCATCATCATC	ACGTTGGATGGACAGGCTCAGATATTTGAG

Table 13

dbSNP rs#	Extend Primer	Term Mix
KIAA0783_SNP1	ATTCAGCACAAGTTGTCA	ACG
KIAA0783_SNP2	GAAAGACCTAGAAAGAAAA	ACT
182594	CTCTCTCTTTCTCTCACT	ACT
190075	GTCTGGAGATCCGAATTT	ACT
218962	GCACCATCTGATTGGCC	ACT
218973	CCCAACACTATCCCTTC	ACG
218980	ATCCAGAAGACAATATTGCATTTA	ACT
218981	GTATTGCTTTGTTGCC	ACG
218983	GGTAAAGAGATGAAGTGC	ACG
220090	CCCAGATATCCTCGGAA	ACT
220091	TGTTACTTATTACATTGTCCAA	ACT
220093	TTATATTCACTCTGAAATCCC	ACT
220095	CACTGTTGCATGAAATGTA	CGT
220096	CCTGCTACAAAGGGACCTCA	ACT
220097	ACAGAGTTTTAAACCTCCTACA	ACT
284856	TACATTGAGGCAGTTTGTGCT	ACG
286243	AGCAATCTAAACATGAGATTGAGC	ACT
220097	ACAGAGTTTTAAACCTCCTACA	ACT
1026903	CTTATCTGTTTACCATACAATCTA	ACG
1154920	CAACACAAAATGCCAATAG	ACG
1154921	TGTGGCTGTATATACGAGTTAA	ACG
1154922	TTGAGGAGAGGAGGTAA	ACT
1154923	CATCAATCTAATCTCATTTCCTAT	ACT
1483201	TGGGTGGTCCTTTTCTGATA	ACG
1483202	TAATCATGTGGAATTTCCAG	ACT
1483204	CAGGCCTGAGCCACTGT	ACT
1640699	CTAATCTGTCTGGTTAATAGAA	ACT
1640700	GCAAAAGCAAAAGTAAGCT	ACT
1640701	AAACAATGGTAATCTAGAGTAAGC	ACT
1640702	TGATTCAATTTCTGTTGACTACT	ACT
1640703	GTGACCTGAGACCACAGATC	ACT
1640705	TCCAAATAAGAAGCCCT	ACT
1640710	CAGTGTAATAAATTATCAGTTCAT	ACT
1681281	TGGAGTTCAATATAAAGATACAC	ACT
1681284	TGTTTTCAGTTTTATTTGCC	ACT
1681286	TTGTCTGCTAGCCATTT	ACT
1681290	AATCAGTGTTTCTTTAAAGGTC	ACT
1681291	CTGGTATTGTATTTTATGGTACT	ACT
1681292	GGGCAACATAGCAAAACCCTG	ACG
1681305	TTCCCAGCCCTACTTAC	ACT
1681311	CTGAGTCCTAAAAAAGGT	ACG
1681312	TTAATACAAGGAAATTCAGC	ACT
2108111	AGAATTTGAAGACATAAAAACC	ACG
2108114	GCGACAGAGCAAGACTC	ACG
2110376	GGGTCAGAGAACTCTATTAA	ACT
2110377	AGAGAACTCTATTAAGTAGGTC	ACT

dbSNP rs#	Extend Primer	Term Mix
2160059	CTCATGGATCTGTCTTAC	ACT
2190295	GGGGAAAAAAGGTCATATTA	ACT
2306768	CTGAAGTGCTGGGATTATGGG	CGT
2353340	TTTTCTGTGCTTTCTTTGT	ACT
2353341	CATCTACTCTCTTTGAAGTT	ACT
2353342	CTTTCTTCCTGACTTACAAATTC	ACT
2353343	GTGTTTTTGTGACATATCAAT	ACT
2510348	GGAGGATGAGTTGTGTTGACT	ACT
2883140	TTGTCTTAACTACTATAAACTGAA	CGT
3801435	GCTATACTCTGTAGGAGTTTATCT	ACG
3801437	CAGTCTCTTGATTTTAAGGA	ACT
3801438	CTCGTACTTTTGCCAC	ACG
3823875	ATTTCAGTGATATAGGAGTCT	ACT

Genetic Analysis of Allelotyping Results

[0256] Allelotyping results are shown for cases and controls in Table 14. The allele frequency for the A2 allele is noted in the fifth and sixth columns for breast cancer pools and control pools, respectively, where “AF” is allele frequency. The allele frequency for the A1 allele can be easily calculated by subtracting the A2 allele frequency from 1 (A1 AF = 1-A2 AF). For example, the SNP rs218973 has the following case and control allele frequencies: case A1 (G) = 0.640; case A2 (A) = 0.360; control A1 (G) = 0.645; and control A2 (A) = 0.355, where the nucleotide is provided in paranthesis. SNPs with blank allele frequencies were untyped.

Table 14

dbSNP rs#	Position in Figure 2	Chromosome Position	A1/A2 Allele	A2 Case AF	A2 Control AF	p-Value
218973	201	10710201	G/A	0.360	0.355	0.8462
218962	6395	10716395	T/C	0.547	0.535	0.6939
1640705	8558	10718558	T/C	0.601	0.568	0.2583
218983	9429	10719429	C/T	0.561	0.558	0.9406
190075	9809	10719809	T/G	0.447	0.428	0.5348
284856	10072	10720072	C/T	0.612	0.585	0.3555
218981	10511	10720511	C/T	0.432	0.363	0.0189
218980	11556	10721556	C/G	0.409	0.471	0.0378
1640703	16857	10726857	A/G	0.841	0.859	0.3809
1640702	16951	10726951	A/G	0.674	0.656	0.5269
1640701	17027	10727027	C/G	0.266	0.270	0.9020
1681305	17177	10727177	T/C	0.422	0.483	0.0406
1640700	17615	10727615	A/C	0.456	0.423	0.2641
1640699	17950	10727950	C/G	0.344	0.370	0.3558
1154923	18329	10728329	T/G	0.885	0.878	0.7144
1154922	18384	10728384	T/C	0.406	0.479	0.0151
1154921	18561	10728561	G/A	0.367	0.365	0.9611
1154920	18579	10728579	C/T	0.284	0.248	0.1803
2510348	18871	10728871	C/G	0.409	0.425	0.5940
1681311	27152	10737152	C/T	0.251	0.279	0.3099
1681312	27306	10737306	T/C	0.303	0.260	0.1171
1681286	28091	10738091	T/C	0.557	0.544	0.6560

dbSNP rs#	Position in Figure 2	Chromosome Position	A1/A2 Allele	A2 Case AF	A2 Control AF	p-Value
1640710	28661	10738661	A/C	0.455	0.515	0.0472
1681284	29011	10739011	T/C	0.418	0.388	0.3124
2110377	29962	10739962	T/G	0.080	0.058	0.1549
2110376	29969	10739969	T/G	0.265	0.313	0.0798
2160059	30085	10740085	T/C	0.066	0.063	0.8793
1681290	31656	10741656	A/G	0.222	0.287	0.0129
1681291	31685	10741685	A/G	0.017	0.042	0.0143
1681292	31749	10741749	G/A	0.335	0.392	0.0458
220091	45389	10755389	T/C	0.245	0.326	0.0034
182594	45459	10755459	G/C	0.238	0.325	0.0017
220090	46647	10756647	A/G	0.332	0.411	0.0066
220097	49860	10759860	T/C	0.258	0.343	0.0025
220096	53061	10763061	T/C	0.240	0.301	0.0214
220095	57308	10767308	T/A	0.618	0.526	0.0026
3801435	61563	10771563	A/G	0.622	0.507	0.0002
1681281	61660	10771660	A/G	0.501	0.433	0.0235
1026903	62212	10772212	C/T	0.855	0.859	0.8503
220093	67090	10777090	T/G	0.564	0.461	0.0009
286243	67198	10777198	T/C	0.591	0.519	0.0170
3801437	70071	10780071	A/G	0.385	0.459	0.0141
3801438	70191	10780191	G/A	0.018	0.022	0.6491
2108111	74006	10784006	C/T	0.360	0.438	0.0090
2353340	75600	10785600	A/G	0.234	0.309	0.0056
3823875	85761	10795761	A/G	0.502	0.409	0.0025
2190295	90798	10800798	T/G	0.319	0.402	0.0045
KIAA0783 SNP1	90883	10800883	C/T	0.309	0.396	0.0030
2306768	91259	10801259	T/A	0.558	0.472	0.0051
2353341	95416	10805416	C/G	0.163	0.248	0.0008
2353342	95446	10805446	T/G	0.118	0.176	0.0068
2883140	96368	10806368	G/T	0.672	0.561	0.0003
2353343	97050	10807050	T/C	0.071	0.075	0.8073
2108114	97362	10807362	C/T	0.433	0.321	0.0003
1483204	97630	10807630	A/C	0.063	0.093	0.0706
1483202	97989	10807989	T/C	0.643	0.567	0.0101
1483201	98107	10808107	C/T	0.688	0.598	0.0022
KIAA0783 SNP2	NOT MAPPED			0.411	0.459	0.1085

[0257] Figure 14 shows the proximal SNPs in and around the KIAA0783 region. The position of each SNP on the chromosome is presented on the x-axis. The y-axis gives the negative logarithm (base 10) of the p-value comparing the estimated allele in the case group to that of the control group. The minor allele frequency of the control group for each SNP designated by an X or other symbol on the graphs in Figure 14 can be determined by consulting Table 14. By proceeding down the Table from top to bottom and across the graphs from left to right the allele frequency associated with each symbol shown can be determined.

[0258] To aid the interpretation, multiple lines have been added to the graph. The broken horizontal lines are drawn at two common significance levels, 0.05 and 0.01. The vertical broken lines are drawn every 20kb to assist in the interpretation of distances between SNPs. Two other lines are drawn to expose linear trends in the association of SNPs to the disease. The light gray line (or generally bottom-most curve) is a nonlinear smoother through the data points on the graph using a local polynomial regression method (W.S. Cleveland, E. Grosse and W.M. Shyu (1992) Local regression models. Chapter 8 of Statistical Models in S eds J.M. Chambers and T.J. Hastie,

Wadsworth & Brooks/Cole.). The black line (or generally top-most curve, *e.g.*, see peak in left-most graph just to the left of position 92150000) provides a local test for excess statistical significance to identify regions of association. This was created by use of a 10kb sliding window with 1kb step sizes. Within each window, a chi-square goodness of fit test was applied to compare the proportion of SNPs that were significant at a test wise level of 0.01, to the proportion that would be expected by chance alone (0.05 for the methods used here). Resulting p-values that were less than 10^{-8} were truncated at that value.

[0259] Finally, the gene or genes present in the loci region of the proximal SNPs as annotated by Locus Link ([http address: www.ncbi.nlm.nih.gov/LocusLink/](http://www.ncbi.nlm.nih.gov/LocusLink/)) are provided on the graph. The exons and introns of the genes in the covered region are plotted below each graph at the appropriate chromosomal positions. The gene boundary is indicated by the broken horizontal line. The exon positions are shown as thick, unbroken bars. An arrow is placed at the 3' end of each gene to show the direction of transcription.

Example 5

DPF3 Proximal SNPs

[0260] It has been discovered that a polymorphic variation (rs1990440) in a gene encoding DPF3 is associated with the occurrence of breast cancer (see Examples 1 and 2). Subsequently, SNPs proximal to the incident SNP (rs1990440) were identified and allelotyped in breast cancer sample sets and control sample sets as described in Examples 1 and 2. A total of forty allelic variants located within or nearby the DPF3 gene were identified and allelotyped. The polymorphic variants are set forth in Table 15. The chromosome position provided in column four of Table 15 is based on Genome "Build 33" of NCBI's GenBank.

Table 15

dbSNP rs#	Chromosome	Position in Figure 3	Chromosome Position	Allele Variants
2052146	14	160	71227260	A/C
2052145	14	6053	71233153	T/G
740980	14	9719	71236819	A/G
758915	14	10481	71237581	T/C
758914	14	10676	71237776	A/T
2098195	14	17179	71244279	C/G
740979	14	18561	71245661	A/T
740978	14	18658	71245758	G/C
740977	14	18694	71245794	A/G
740976	14	18858	71245958	T/C
2052143	14	24582	71251682	G/A
2052142	14	24683	71251783	G/A
2052141	14	24767	71251867	C/T
758913	14	27402	71254502	A/G
740975	14	28150	71255250	T/G
747987	14	28494	71255594	T/C

dbSNP rs#	Chromosome	Position in Figure 3	Chromosome Position	Allele Variants
1126160	14	32003	71259103	A/C
2332918	14	35588	71262688	C/T
2332919	14	35619	71262719	T/C
1990443	14	35856	71262956	G/A
3937455	14	36254	71263354	G/C
973963	14	37314	71264414	G/A
1990441	14	40033	71267133	T/G
1990440	14	40095	71267195	G/C
2159715	14	42593	71269693	A/C
2109795	14	42799	71269899	A/G
2159714	14	43090	71270190	G/A
1468662	14	46683	71273783	A/G
2215591	14	49774	71276874	A/G
2109794	14	51796	71278896	C/T
2877821	14	52079	71279179	A/T
2191822	14	53857	71280957	T/C
2191821	14	53971	71281071	A/C
1544579	14	55899	71282999	T/C
2215590	14	60682	71287782	G/A
1004552	14	61291	71288391	C/T
1860749	14	72720	71299820	G/A
1860748	14	72752	71299852	A/C
763388	14	85507	71312607	A/G
1035099	14	89751	71316851	T/A

Assay for Verifying and Allelotyping SNPs

[0261] The methods used to verify and allelotype the sixty-three proximal SNPs of Table 15 are the same methods described in Examples 1 and 2 herein. The PCR primers and extend primers used in these assays are provided in Table 16 and Table 17, respectively.

Table 16

dbSNP rs#	Forward PCR primer	Reverse PCR primer
740975	ACGTTGGATGGAAACCAAGATAGGAAATGG	ACGTTGGATGCTCAGTGCCAGAAATACCAG
740976	ACGTTGGATGTCCTGTTTCTAAGCAGGGAG	ACGTTGGATGATCAGGACTACCTGAGCAAC
740977	ACGTTGGATGTCCAGTGAGGCCTCCCTCCAA	ACGTTGGATGCAGCAACCCAAAGCAACACG
740978	ACGTTGGATGTAGCCACGCCATTATTGGAG	ACGTTGGATGCTTCACATCCCTCCTCAAAG
740979	ACGTTGGATGATCCTAACCAGGTCTGATGG	ACGTTGGATGAAGGGCCAAGCAATGCTTTG
740980	ACGTTGGATGGGTAGGGCTGTCTGTTTCAT	ACGTTGGATGATGCCTGCCACATTGGGTAA
747987	ACGTTGGATGAGGTCTGGCACTGCTAAATG	ACGTTGGATGCCTTGTGAACCTTCCAACCTG
758913	ACGTTGGATGCCTAGCCAACATCCTTTTCC	ACGTTGGATGAGCAACCAAGTCTAGTTTTCG
758914	ACGTTGGATGCCCTTGTTTTAGAGGTTGGG	ACGTTGGATGTGTGATCCAGACATCAGCTC
758915	ACGTTGGATGCAAGAAGGGCATTCTACCC	ACGTTGGATGCAATGCTGCTGACATCAGAC
763388	ACGTTGGATGGGGTACTCTTAGCTGAGAAC	ACGTTGGATGTACAGGGATTGTGATGTGGG
973963	ACGTTGGATGGATTTGTTCTGGCAGGAATG	ACGTTGGATGACAAACCACTAAACTTTTCAG
1004552	ACGTTGGATGGATCATCCAAGTATGCTCCC	ACGTTGGATGGCAAAACCCAGTGCCAAAAC

dbSNP rs#	Forward PCR primer	Reverse PCR primer
1035099	ACGTTGGATGAAAGGGTACCCAGACTTCAC	ACGTTGGATGTGGGGAGAACTTTGGTCAAC
1126160	ACGTTGGATGGGGTTCTCTCTTGACAGATG	ACGTTGGATGTGTTCTCACCCCTGTTCTGTT
1468662	ACGTTGGATGGCTAGAAATCACCAGCAACC	ACGTTGGATGTCATGTAGGTTGGCTCTGAC
1544579	ACGTTGGATGACCATTATCATCTTCCCAGG	ACGTTGGATGCCTTATCTCTCTAAGACATGC
1860748	ACGTTGGATGACTCGACTAGCTAGTCTTGG	ACGTTGGATGAAAGCAATCCAGCGGACAAG
1860749	ACGTTGGATGTCCCCGGAATGATACATGAC	ACGTTGGATGAACATGATTAAGGATAAAGC
1990440	ACGTTGGATGAAGTCACTAACCCACACAC	ACGTTGGATGCCAGGGTGTGTTCTAATACG
1990441	ACGTTGGATGTCAGAGATATGCACTGCAAG	ACGTTGGATGCACACCCTGGCATGAATGTG
1990443	ACGTTGGATGCACTGGATTGGCAAGAAGG	ACGTTGGATGTACATGATCCTCCCCTCTAC
2052141	ACGTTGGATGCCTGCAAAATCCCTCATACC	ACGTTGGATGATAGAAGCGTGACCTTACCC
2052142	ACGTTGGATGGGTATGAGGGATTTTGACAGG	ACGTTGGATGACTGGACTCACCCACATAAG
2052143	ACGTTGGATGCCAGTGTAAACACAAGGGTC	ACGTTGGATGTGTGTCACTTCTACCTCCAC
2052145	ACGTTGGATGGTGCTGGCTGCCTAGTTCTA	ACGTTGGATGGGCTTCTCAATTCAGATGGG
2052146	ACGTTGGATGCCACAAAAGCACGTGATTTT	ACGTTGGATGTTATTTGAGCTCTGATAGTG
2098195	ACGTTGGATGGCTCCAGTCTCTAATCACAC	ACGTTGGATGCAAAGTTCTCTGCCTGAGTG
2109794	ACGTTGGATGTAATCCCAGCACTTTGGGAG	ACGTTGGATGAGGCTGATCTTGAACCTCTG
2109795	ACGTTGGATGCAAACAAGGTCCCAGCATTC	ACGTTGGATGTCCTGACTCTCTCAAAACCC
2159714	ACGTTGGATGAAACTCTCTCGTTGCTGTGG	ACGTTGGATGAAAGCCCCTCTAGCAAAGG
2159715	ACGTTGGATGCTGCCTGCAAGTTCCCATTG	ACGTTGGATGTACAGGCACTGGCGAAGAAG
2191821	ACGTTGGATGGAAAGTGTCTTAGCTTGCC	ACGTTGGATGTGAGATGGATCTGGAGCCAC
2191822	ACGTTGGATGATTTTTCCCGGCATCTGACC	ACGTTGGATGTGCAAAGTGGTGGAGGAAAG
2215590	ACGTTGGATGTCCAAGAAGGACAGCAGTAG	ACGTTGGATGATGAGAGCCTTTCTTCAGGG
2215591	ACGTTGGATGATTTGTTAAATTCATAGAAC	ACGTTGGATGTCCCCAGTTTGCATCTTGAC
2332918	ACGTTGGATGAACCCATGGGACCACAATTC	ACGTTGGATGTAGGATGGGTGTTTCCTAGC
2332919	ACGTTGGATGTCTGAGGGCTCTCTCTAATG	ACGTTGGATGATGAAGGAAGAAGCCCTGAC
2877821	ACGTTGGATGATAATCTATGTCCTAGATTG	ACGTTGGATGTAGTAGCATTCCAAGTGCCC
3937455	ACGTTGGATGGCAAGAATAGGTTCTTTCGC	ACGTTGGATGACCTCCACACTCATTACCTC

Table 17

dbSNP rs#	Extend Primer	Term Mix
740975	ACCAGCTCTCTTTGGAT	ACT
740976	ATCCAGATGGCCCTGAC	ACT
740977	TGGTTTTCGAATAAGTAGCCAC	ACT
740978	AAGCCTTCCTATCCCCA	ACT
740979	TGCTTTGGGGCAGACTGAC	CGT
740980	CACATTGGGTAAATGATGA	ACT
747987	AACCTGGTTCTGCCATT	ACT
758913	CCAGTCTAGTTTTCGATCACC	ACT
758914	CCCCAGTGATCCTGAGAAAT	CGT
758915	GACATCAGACCTATGCCAGGA	ACT
763388	CACTCATGCCTCAAGCCAAT	ACT
973963	AACAACCAACTCTCCAG	ACG
1004552	TCTTGGCTCAGTGCTGC	ACG
1035099	TTGGTCAACATCGCAGC	CGT
1126160	GAAGCCCATCGCTAAGTGTTT	ACT

dbSNP rs#	Extend Primer	Term Mix
1468662	CTCTGACTGAGGAGAGACC	ACT
1544579	GACATGCATCAAAGCAGCTG	ACT
1860748	TCTTGGAGCCATATTTTATTTG	ACT
1860749	TTAAGGATAAAGCAATCCAG	ACG
1990440	CGTCAGCAAATGTGTACCGA	ACT
1990441	CATGAATGTGATTACATTCTCC	ACT
1990443	TTCCCCTCAGCTCTTAG	ACG
2052141	CTTACCCCCAAAGATGTCCA	ACG
2052142	AGCCAGGATAATCTCCTCA	ACG
2052143	TCTACCTCCACTTCCAA	ACG
2052145	ATTCAGATGGGATCACAGAAG	ACT
2052146	GAGCTCTGATAGTGATTGTGAGT	ACT
2098195	TAAACCTTTCTATGTTCCCTG	ACT
2109794	CTCAGGTGATCCACCCA	ACG
2109795	TCCCAGAATTTGGAGCC	ACT
2159714	CAAAAGGATCTGCAAAAG	ACG
2159715	CATAGGGATAGGAATGGG	ACT
2191821	ATGTGGGTTTGGACTGGGGCT	ACT
2191822	AGGAAAGGAATGTCTGCCCC	ACT
2215590	CAGGGCCAGCCATGAACGT	ACG
2215591	TTCAATAAAATGTACTCATTCAA	ACT
2332918	TCTCTCTAATGGGGACC	ACG
2332919	ACTGGATCCCAGAAGAG	ACT
2877821	CCCTGTTCTGCACCTTTAAA	CGT
3937455	TCCTTTTTTCCCCACCC	ACT

Genetic Analysis of Allelotyping Results

[0262] Allelotyping results are shown for cases and controls in Table 18. The allele frequency for the A2 allele is noted in the fifth and sixth columns for breast cancer pools and control pools, respectively, where “AF” is allele frequency. The allele frequency for the A1 allele can be easily calculated by subtracting the A2 allele frequency from 1 (A1 AF = 1-A2 AF). For example, the SNP in row 2 of Table 13 (rs2052146) has the following case and control allele frequencies: case A1 (A) = 0.990; case A2 (C) = 0.010; control A1 (A) = 0.948; and control A2 (C) = 0.052, where the nucleotide is provided in parenthesis. SNPs with blank allele frequencies were untyped (“not AT”).

Table 18

dbSNP rs#	Position in Fig 3	Chrom Position	Alleles (A1/A2)	A2 Case AF	A2 Control AF	p-Value
2052146	160	71227260	A/C	0.010	0.042	0.0014
2052145	6053	71233153	T/G	0.858	0.776	0.0007
740980	9719	71236819	A/G	0.620	0.644	0.4134
758915	10481	71237581	T/C	0.718	0.718	0.9903
758914	10676	71237776	A/T	0.754	0.749	0.8560
2098195	17179	71244279	C/G	0.976	0.989	0.1034
740979	18561	71245661	A/T	0.656	0.694	0.1850

dbSNP rs#	Position in Fig 3	Chrom Position	Alleles (A1/A2)	A2 Case AF	A2 Control AF	p-Value
740978	18658	71245758	G/C	0.011	0.047	0.0005
740977	18694	71245794	A/G	0.913	0.873	0.0353
740976	18858	71245958	T/C	0.610	0.676	0.0217
2052143	24582	71251682	G/A	0.466	0.405	0.0418
2052142	24683	71251783	G/A	0.015	0.051	0.0011
2052141	24767	71251867	C/T	0.363	0.315	0.0950
758913	27402	71254502	A/G	0.931	0.871	0.0011
740975	28150	71255250	T/G	0.461	0.514	0.0763
747987	28494	71255594	T/C	0.715	0.813	0.0003
1126160	32003	71259103	A/C	0.349	0.409	0.0392
2332918	35588	71262688	C/T	0.041	0.070	0.0355
2332919	35619	71262719	T/C	0.300	0.271	0.2797
1990443	35856	71262956	G/A	0.324	0.268	0.0407
3937455	36254	71263354	G/C	0.445	0.455	0.7518
973963	37314	71264414	G/A	0.029	0.035	0.6030
1990441	40033	71267133	T/G	0.128	0.152	0.2380
1990440	40095	71267195	G/C	0.744	0.842	0.0002
2159715	42593	71269693	A/C	0.534	0.542	0.7822
2109795	42799	71269899	A/G	0.795	0.747	0.0582
2159714	43090	71270190	G/A	0.035	0.036	0.9187
1468662	46683	71273783	A/G	0.035	0.069	0.0118
2215591	49774	71276874	A/G	0.892	0.857	0.0776
2109794	51796	71278896	C/T	0.042	0.041	0.9714
2877821	52079	71279179	A/T	0.778	0.862	0.0005
2191822	53857	71280957	T/C	0.899	0.845	0.0078
2191821	53971	71281071	A/C	0.427	0.422	0.8733
1544579	55899	71282999	T/C	0.496	0.483	0.6724
2215590	60682	71287782	G/A	0.271	0.285	0.5936
1004552	61291	71288391	C/T	0.393	0.378	0.5996
1860749	72720	71299820	G/A	0.652	0.522	0.0001
1860748	72752	71299852	A/C	0.894	0.820	0.0007
763388	85507	71312607	A/G	0.291	0.310	0.4883
1035099	89751	71316851	T/A	0.555	0.543	0.7079

[0263] Figure 15 shows the proximal SNPs in and around the DPF3 gene. As indicated, some of the SNPs were untyped. The position of each SNP on the chromosome is presented on the x-axis. The y-axis gives the negative logarithm (base 10) of the p-value comparing the estimated allele in the case group to that of the control group. The minor allele frequency of the control group for each SNP designated by an X or other symbol on the graphs in Figure 15 can be determined by consulting Table 18. By proceeding down the Table from top to bottom and across the graphs from left to right the allele frequency associated with each symbol shown can be determined.

[0264] To aid the interpretation, multiple lines have been added to the graph. The broken horizontal lines are drawn at two common significance levels, 0.05 and 0.01. The vertical broken lines are drawn every 20kb to assist in the interpretation of distances between SNPs. Two other lines are drawn to expose linear trends in the association of SNPs to the disease. The light gray line (or generally bottom-most curve) is a nonlinear smoother through the data points on the graph using a local polynomial regression method (W.S. Cleveland, E. Grosse and W.M. Shyu (1992) Local regression models. Chapter 8 of Statistical Models in S eds J.M. Chambers and T.J. Hastie, Wadsworth & Brooks/Cole.). The black line (or generally top-most curve, *e.g.*, see peak in left-most

graph just to the left of position 92150000) provides a local test for excess statistical significance to identify regions of association. This was created by use of a 10kb sliding window with 1kb step sizes. Within each window, a chi-square goodness of fit test was applied to compare the proportion of SNPs that were significant at a test wise level of 0.01, to the proportion that would be expected by chance alone (0.05 for the methods used here). Resulting p-values that were less than 10^{-8} were truncated at that value.

[0265] Finally, the gene or genes present in the loci region of the proximal SNPs as annotated by Locus Link ([http address: www.ncbi.nlm.nih.gov/LocusLink/](http://www.ncbi.nlm.nih.gov/LocusLink/)) are provided on the graph. The exons and introns of the genes in the covered region are plotted below each graph at the appropriate chromosomal positions. The gene boundary is indicated by the broken horizontal line. The exon positions are shown as thick, unbroken bars. An arrow is placed at the 3' end of each gene to show the direction of transcription.

Example 6

CENPC1 Proximal SNPs

[0266] It has been discovered that a polymorphic variation (rs355510) in the CENPC1 region is associated with the occurrence of breast cancer (see Examples 1 and 2). Subsequently, SNPs proximal to the incident SNP (rs355510) were identified and allelotyped in breast cancer sample sets and control sample sets as described in Examples 1 and 2. Approximately seventy-nine allelic variants located within the CENPC1 region were identified and allelotyped. The polymorphic variants are set forth in Table 19. The chromosome position provided in column four of Table 19 is based on Genome "Build 33" of NCBI's GenBank.

Table 19

dbSNP rs#	Chromosome	Position in Figure 4	Chromosome Position	Allele Variants
1874633	4	196	68275196	A/G
1846060	4	13311	68288311	G/A
451352	4	14486	68289486	C/T
355468	4	14691	68289691	A/T
355469	4	15551	68290551	C/G
355470	4	17702	68292702	T/C
355471	4	17872	68292872	T/C
191650	4	19588	68294588	T/C
355472	4	19910	68294910	T/A
1874635	4	20006	68295006	A/C
1497430	4	20575	68295575	A/G
2254659	4	21092	68296092	G/A
3822197	4	22830	68297830	C/T
2632453	4	23455	68298455	A/G
2646282	4	23716	68298716	G/A
2646285	4	23890	68298890	T/G
768244	4	24001	68299001	C/T
724199	4	24995	68299995	G/A

dbSNP rs#	Chromosome	Position in Figure 4	Chromosome Position	Allele Variants
1187960	4	27282	68302282	T/C
1187961	4	27779	68302779	C/T
355518	4	29099	68304099	C/G
355519	4	31185	68306185	A/G
355511	4	33994	68308994	C/T
451397	4	34942	68309942	T/C
355513	4	35137	68310137	C/G
355514	4	36538	68311538	T/C
355515	4	37139	68312139	C/T
1056789	4	37358	68312358	G/A
2646290	4	38828	68313828	A/G
190255	4	39469	68314469	T/C
355466	4	40233	68315233	T/C
355465	4	40472	68315472	A/T
2646292	4	41679	68316679	C/T
2632454	4	41682	68316682	G/A
1056787	4	42831	68317831	A/G
CENPC1_SNP1	4	42976	68317976	A/G
173317	4	44128	68319128	A/G
451344	4	44195	68319195	C/T
355510	4	46769	68321769	G/A
355508	4	47363	68322363	G/C
451391	4	48843	68323843	C/T
355500	4	52574	68327574	A/G
355499	4	52602	68327602	A/G
355498	4	53212	68328212	A/G
1187974	4	53781	68328781	C/G
355493	4	54710	68329710	A/T
2632456	4	55808	68330808	G/A
1825790	4	57987	68332987	T/A
355475	4	58556	68333556	C/A
1391110	4	59148	68334148	T/A
1442557	4	59286	68334286	G/C
355478	4	60217	68335217	A/G
189579	4	60412	68335412	G/T
355480	4	60753	68335753	C/T
355481	4	60791	68335791	T/G
355483	4	61524	68336524	A/G
355485	4	62543	68337543	T/C
2646267	4	62825	68337825	A/G
2646268	4	62826	68337826	A/C
355486	4	62857	68337857	C/T
355487	4	63400	68338400	T/C
355488	4	63960	68338960	T/A
355489	4	64307	68339307	A/G
451376	4	64539	68339539	A/G
1353626	4	65728	68340728	A/G
2632450	4	66000	68341000	G/A
2646269	4	66521	68341521	T/G
2276945	4	68185	68343185	C/T

dbSNP rs#	Chromosome	Position in Figure 4	Chromosome Position	Allele Variants
3775861	4	69643	68344643	G/A
1403151	4	74909	68349909	C/A
1843833	4	82973	68357973	T/G
1843831	4	83039	68358039	T/C
3806810	4	85713	68360713	A/G
3775862	4	86873	68361873	T/C
1962700	4	90293	68365293	T/G
2046601	4	91810	68366810	T/G
2171386	4	92609	68367609	A/G
2046599	4	92884	68367884	G/A
355490	4			A/T

Assay for Verifying and Allelotyping SNPs

[0267] The methods used to verify and allelotype the proximal SNPs of Table 19 are the same methods described in Examples 1 and 2 herein. The PCR primers and extend primers used in these assays are provided in Table 20 and Table 21, respectively.

Table 20

dbSNP rs#	Forward PCR primer	Reverse PCR primer
1056787	ACGTTGGATGCATTTTCATATTTGTAGATC	ACGTTGGATGTCTCAGCCCTCTGATAAAAC
1056789	ACGTTGGATGTGAAGGTTCTGGAGGTATCG	ACGTTGGATGTCTTCTTAGCCAAGTCTGCC
CENPC1 SNP1	ACGTTGGATGAACAACGCACAATATCCCCG	ACGTTGGATGGGGTGAGGTTTATGGGAATG
11250	ACGTTGGATGAACAACGCACAATATCCCCG	ACGTTGGATGCATTTGCCAAAGTCTTAGGT
1187960	ACGTTGGATGTGAACCCTTCAAAATCACCC	ACGTTGGATGTTGTGTTTCATGGGAGGAGG
1187961	ACGTTGGATGCAACAGATTTTCCCTGTAGAC	ACGTTGGATGTGCATTGACTTCTCCTCAGC
1187974	ACGTTGGATGGCTGAGCAGAAGCTCTTTCA	ACGTTGGATGTGGGCAAAGACTTCATGATT
1353626	ACGTTGGATGCAACTACTACCTAGATGATGA	ACGTTGGATGAATAGAAAATCTAAATTGTCTAC
1391110	ACGTTGGATGAGTATGAAGGTCAGGGTCAG	ACGTTGGATGAAAGAGCACTGACCATGGAG
1403151	ACGTTGGATGTCAGTCAGAGATCATAGTTC	ACGTTGGATGCATGTAGTGCTTTAACAAATG
1442557	ACGTTGGATGCAACACATGCACCATTAGCG	ACGTTGGATGGAAGCCACAAACAGATCAGG
1497430	ACGTTGGATGTTGCTTGCTTGATGATTGGC	ACGTTGGATGTCTTCTGGACTTTAGCACTG
173317	ACGTTGGATGCTATAGGACTGTAAATTGTAG	ACGTTGGATGTTTTTACACACATGCTGTCA
1825790	ACGTTGGATGGGCCAACATGGTAAACTCC	ACGTTGGATGCTGGGATAACAGGTACTTGC
1843831	ACGTTGGATGTCTCAGCTCATTTCCACCTC	ACGTTGGATGACCTGTAGTCCCAGCTACTC
1843833	ACGTTGGATGGACCAACATGGTGAAATCTC	ACGTTGGATGTGAGTAGCTGGGACTACAGG
1846060	ACGTTGGATGAAGATTATCACCGCACTGGG	ACGTTGGATGATCTCCTGACCTCGTGATCC
1874633	ACGTTGGATGAGGTTTTTGGTATGGTTAGC	ACGTTGGATGGAAAAGGGAGTTGGCCTAAA
1874635	ACGTTGGATGAGAGAGAGAGAGAGAGAGAG	ACGTTGGATGATGGGCTATAGTGGGATAGG
189579	ACGTTGGATGACACCAAAGCAATGGCAAC	ACGTTGGATGGTTGCCTGTTCACTCTGATG
190255	ACGTTGGATGGAGATCTAGCACATTTATCC	ACGTTGGATGAGGTTGCCTGAAATGCTAAG
191650	ACGTTGGATGGAGATACCTTTGCTAAGGTG	ACGTTGGATGGGTAGTAATAATGGTACTCC
1962700	ACGTTGGATGATAAGAGAGAGTGTGGGTGG	ACGTTGGATGATTTCTGACCTCGTGATCC
2046599	ACGTTGGATGTATTGAATTCCTCTGTATG	ACGTTGGATGTCATTCTTTTGAGACTGAAC
2046601	ACGTTGGATGGCTCCAATGACTAAGTGGAC	ACGTTGGATGGACAGAACACTAAGAGCCTA
2171386	ACGTTGGATGCTTATCGAAATGAAATCAAG	ACGTTGGATGACAGCTGCAAACCTAAGGAC

dbSNP rs#	Forward PCR primer	Reverse PCR primer
2254659	ACGTTGGATGATCTCTAAGTGAGATAGAGG	ACGTTGGATGCCAGTCAAATGAAACCCAC
2276945	ACGTTGGATGGGGAATTCTATATCCCATTG	ACGTTGGATGCCCAATTCCAACAGAAAATATC
2632450	ACGTTGGATGTTGAGACAAGCCTAGGCAAC	ACGTTGGATGGTGCTGGGATTACAGGTGTG
2632453	ACGTTGGATGAAAAGTGAGAGGGCAATAGG	ACGTTGGATGCATAGTAAGTCACCACAAGC
2632454	ACGTTGGATGTTCTGTGGGTCAGATGTCTC	ACGTTGGATGAGAAACAGACTTCCTCCAG
2632456	ACGTTGGATGCCACCATATCAACAGATCAG	ACGTTGGATGCCTGCCAGTATGCTGAGAAT
2646267	ACGTTGGATGTGAGAAAAAGCACTCCTGGG	ACGTTGGATGAGGCTGAGACAGGAGAATTG
2646268	ACGTTGGATGCAGGAGAATTGCTTGAACCC	ACGTTGGATGTGAGAAAAAGCACTCCTGGG
2646269	ACGTTGGATGACCACTATTGTTTCTTTCTC	ACGTTGGATGGGCTAAAGAGTGAAACCCTG
2646282	ACGTTGGATGGATTGTTTTGAGTCATCTAC	ACGTTGGATGCTGAAATTGACCAGGAAACAC
2646285	ACGTTGGATGGGTGGATTGGACAAACTTGC	ACGTTGGATGCCTTTTGCTTTTCATTGCTC
2646290	ACGTTGGATGGATAGCAAGCTACCTAAGAC	ACGTTGGATGCCTCCTTACTCCACTCAATC
2646292	ACGTTGGATGTTCTGTGGGTCAGATGTCTC	ACGTTGGATGCAAAGAAACAGACTTCCTCC
355465	ACGTTGGATGTATGAGGTTCTGCCACCAAG	ACGTTGGATGTACCAAATCTGAGGGTAGTC
355466	ACGTTGGATGCAGGAGCTGCTTAATTCCTC	ACGTTGGATGGATCTTGGGCCTAAGTCTC
355468	ACGTTGGATGCCTCTCCTCATTTCTGTAAAC	ACGTTGGATGGGCAGGTGGTTAGCATTAAAG
355469	ACGTTGGATGTTGGGATCTAGGCATCAAGG	ACGTTGGATGAGGAGGCACATAATGCTTGG
355470	ACGTTGGATGACATACACACACACACACAC	ACGTTGGATGGAGACATACACCTCTGCAAC
355471	ACGTTGGATGCTCATTACAACCTCAGCCAG	ACGTTGGATGACTCAGGACTAAGCTAGTTG
355472	ACGTTGGATGTCTCTCTCTCTCTCTCTCTC	ACGTTGGATGCAGCCCTTAGTACTCAATGG
355475	ACGTTGGATGCTGTCTTATCCCAACTTAGA	ACGTTGGATGGTCATGTTACATACCGAAAC
355478	ACGTTGGATGGGAGGAATCCATATATAGGC	ACGTTGGATGCTGCTGAAGGGAATGAGTAC
355480	ACGTTGGATGGTTTACAGTCCCACCAACAG	ACGTTGGATGAGTCAGGAAACAACAGGTGC
355481	ACGTTGGATGATTGCCACACTGTCTTCCAC	ACGTTGGATGGGATGTGGAGAAACAGGAAC
355483	ACGTTGGATGCCATGTAAGTCTGTCAATTA	ACGTTGGATGAAGTGGTAGCAGAAGTGTGG
355485	ACGTTGGATGAAGAAGAGGCATGCAAACAG	ACGTTGGATGCTGCGACAAAAGACACATTG
355486	ACGTTGGATGTGAGAAAAAGCACTCCTGGG	ACGTTGGATGAGGAGAATTGCTTGAACCCG
355487	ACGTTGGATGCGAGGTAATGAGCAAAGTAAG	ACGTTGGATGGACATTAGGTTTCATCTAACCC
355488	ACGTTGGATGCCAGTTTTCTATGACAAACG	ACGTTGGATGAAAGAGCAGGGACAGCAAAG
355489	ACGTTGGATGACTCTAGGTATTTGACTCC	ACGTTGGATGAACTCCATAGTAGAAAGCC
355490	ACGTTGGATGAACTTCCATAGTAGAAAGCC	ACGTTGGATGACTCTAGGTATTTGACTCC
355493	ACGTTGGATGAGTGGTTTGCTGCACCTATC	ACGTTGGATGGGGAGAGCATTAGGACAAAC
355498	ACGTTGGATGATGAGAGAGGACACAAAGAG	ACGTTGGATGTTACTTTGCACAGTGTGGCC
355499	ACGTTGGATGCAATCAAGCAGAAGGATGGG	ACGTTGGATGGGTGTCTTCTTATAGTTGTC
355500	ACGTTGGATGCAATCAAGCAGAAGGATGGG	ACGTTGGATGGGTGTCTTCTTATAGTTGTC
355508	ACGTTGGATGGTGTAGATGTGTATCAGGTCA	ACGTTGGATGGTCCACAAAGCATAGCATCC
355510	ACGTTGGATGCCCTCCTTTTAACCTTTTAGG	ACGTTGGATGTTCTGAGATGATCCTGATGG
355511	ACGTTGGATGCAGGAGGATATGTGAAAGTC	ACGTTGGATGGTGGATACCAAATCCAAGG
355513	ACGTTGGATGTGCTGTATAACAGATTACCC	ACGTTGGATGAACTAGCTAGCTAAGCCTCC
355514	ACGTTGGATGCCTCAATAGGTTGTTGGAAC	ACGTTGGATGTTGAGTTCATACTATGTGCC
355515	ACGTTGGATGAGCTCTGCACTCTGACATAC	ACGTTGGATGGTGCAGAGTACTACTTTGCC
355518	ACGTTGGATGTGCCATGGGTTGTAAAATC	ACGTTGGATGACACAGAGACCAGCTGAAAG
355519	ACGTTGGATGGGGAAGAAGCAGATTTTGAG	ACGTTGGATGCATAGGTTGAGAACATCAAGC
3775861	ACGTTGGATGCCATCTCTTTGAAAATTCCAC	ACGTTGGATGCCCTCAAGTACTTGTTTTGTC
3775862	ACGTTGGATGTAATGAAGCTGAGTTTATTC	ACGTTGGATGGTTTTTTGTTTATTGGTGTCC
3806810	ACGTTGGATGTCTTTTCTCCCATCATTTCC	ACGTTGGATGACTCAATGGTTGCATGTAGG
3822197	ACGTTGGATGTGTTTGCTAAAGCTATGCTG	ACGTTGGATGTGAGCATTATGCCTAAGAGC
451344	ACGTTGGATGCCTTTCTAGATACACTCCAT	ACGTTGGATGCAGCATGTGTGTAATAATGC
451352	ACGTTGGATGAGGCAAATTATTTTGGATG	ACGTTGGATGCTCCCTAAATGGGGAAAAAAG
451362	ACGTTGGATGCAACACATGCACCATTAGCG	ACGTTGGATGGAAGCCACAAACAGATCAGG

dbSNP rs#	Forward PCR primer	Reverse PCR primer
451376	ACGTTGGATGAGCAGTCTATTCTGGTTCAC	ACGTTGGATGGCCTTTGAGCTTTAAAAATC
451391	ACGTTGGATGTAAAGTAGGGACTGGGATGG	ACGTTGGATGGCTGTAGAGTAGTGAAACCC
451397	ACGTTGGATGGTTGCCATATTCAGCAGCTG	ACGTTGGATGCTGTTTCCAGTAGACCTTAG
724199	ACGTTGGATGCCAGCTAAACTGCAAATAC	ACGTTGGATGTGGACTCATTTGAGAATATG
768244	ACGTTGGATGTAAACCCCTTCCTCATCCC	ACGTTGGATGACCTTTAGCAGCCTGAAACC

Table 21

dbSNP rs#	Extend Primer	Term Mix
355469	GCACATAATGCTTGGTTGTATT	ACT
CENPC1_SNP1	CTTGACTTTCTACCTTGAA	ACT
11250	CTCTTGACTTTCTACCTTGAA	ACT
173317	ACTTAGCGGCTTAAACAAC	ACT
189579	CTGTTCACTCTGATGGTAGTTT	CGT
190255	GTACTATGTGGCAGATGA	ACT
191650	GGTACTCCTACTTAAATTTTG	ACT
355465	GAGGGTAGTCTTGGGAACC	CGT
355466	CTCTAGTGAGCTTCCCT	ACT
355468	AGCATTAAGTATTCATGAGAGTTC	CGT
355470	GGTCTGTTTTATATGTGTGT	ACT
355471	AGCTAGTTGCTTCAGTAAGT	ACT
355472	GTACAGTCATAACAGTTGTAA	CGT
355475	TACATACCGAAACACATTCC	CGT
355478	ACATTCTATATGGCCCCTTG	ACT
355480	GGAGAGGATGTGGAGAAA	ACG
355481	GGTGGGACTGTAAACTA	ACT
355483	AGAAGTGTGGACACAGTATC	ACT
355485	CACATTCAACTATACACGCTTTTA	ACT
355486	GTGAGCCGAAATCGTGCCAC	ACG
355487	TTCATCTAACCCTTTTCATAA	ACT
355488	AGCAAAGCTGAAAATGATAA	CGT
355489	CAATAAATAATAGCAAAGACTGG	ACT
355490	TGTTTATATTGCTGTTTCTTGA	CGT
355493	CTCATGTGGGGCTTAAA	CGT
355498	GTGTGGCCATTTTCACT	ACT
355499	TGTTAGATAGAGGTTTATCATTTT	ACT
355500	TTTTTCCTGCAATAGTTTCT	ACT
355508	ATACTTATGCTCTGCTACC	ACT
355510	ATGGTTTCTTTCTTGTCCTTC	ACG
355511	GGATGCTCAAGTCCCTTATATA	ACG
355513	GCCTCCCAGATTGCTGA	ACT
355514	TGTGCCAAATATTTGCTAGAT	ACT
355515	ACTACTTTGCCTGTGTGTCA	ACG
355518	ACCAGCTGAAAGAAAATC	ACT
355519	AAGCTTAGTATGTCCAAATCTAAC	ACT
451344	GTGTGTAAAAATGCATTCCAAGTT	ACG

dbSNP rs#	Extend Primer	Term Mix
451352	CCCCCGAAATGTTTCAAAGG	ACG
451362	CCACAAACAGATCAGGTTGGTG	ACT
451376	AGTATGTAAAAAGATAGGGAAGA	ACT
451391	GAGTAGTGAAACCCCTGACC	ACG
451397	CAGTAGACCTTAGTTTCTTAACC	ACT
724199	GAGAATATGATAAAAGCTCAGACC	ACG
768244	GTTTCTGTCTCTGGCGA	ACG
1056787	GGATACAAGTTATGCTTTGATAG	ACT
1056789	TCCAATGGCTCACTCAG	ACG
1187960	GGAGGAGGTCAAAATATCA	ACT
1187961	GACTTCTCCTCAGCTATGAA	ACG
1187974	TGATTAAAACACCAAAAGCAATT	ACT
1353626	AATCTAAATTGTCTACTGAACT	ACT
1391110	CCATGGAGTTGTAAGGAA	CGT
1403151	TAGTGCTTTAACAAATGCTGTCA	CGT
1442557	CACAAACAGATCAGGTTGGTG	ACT
1497430	GAATTGGGGAGAGAAAGGGA	ACT
1825790	CCTGGCAAATTTTGGTATTTTAG	CGT
1843831	GCGGGAGAATGGCATGA	ACT
1843833	GCTCACCACCACACCTG	ACT
1846060	AAAGTGCTGGGATTACAGG	ACG
1874633	TGGCCTAAAAATATTTTACCGT	ACT
1874635	CAACTGTTTAACAACCAGGC	ACT
1962700	AGAGTGCTGGGATTACA	ACT
2046599	CTTTTGAGACTGAACACCTCTA	ACG
2046601	AGAACACTAAGAGCCTAGAATGG	ACT
2171386	AGTATGCAGAGACTTACAG	ACT
2254659	AACCCACCATTCTCTATG	ACG
2276945	CACAAAATACCTCCAAATTTTA	ACG
2632450	TTACAGGTGTGAGCCAC	ACG
2632453	CACCACAAGCCACTTGA	ACT
2632454	CTTCCTCCCAGAGCCAC	ACG
2632456	TCATAGGTAATGTGGATTTTGT	ACG
2646267	TTGCTTGAACCCGGGAG	ACT
2646268	TCGGCTCACTGCAATCTCT	ACT
2646269	TTCTCGCAAAGAGAAAAC	ACT
2646282	GGAATTAGCAGTCATTTCTTA	ACG
2646285	ATTTCTCTAGACTTTGCTACAAT	ACT
2646290	AGTTCATCCTTCAGGAA	ACT
2646292	AGACTTCCTCCCAGAGC	ACG
3775861	GTTTTGTCTTCAAATAGTAAAGA	ACG
3775862	TCCATTTTTATTTGCAGAAGAC	ACT
3806810	ATTGGATTTGGCGTAGC	ACT
3822197	AGCAGTAGGCAACTTCT	ACG

Genetic Analysis of Allelotyping Results

[0268] Allelotyping results are shown for cases and controls in Table 22. The allele frequency for the A2 allele is noted in the fifth and sixth columns for breast cancer pools and control pools, respectively, where "AF" is allele frequency. The allele frequency for the A1 allele can be easily calculated by subtracting the A2 allele frequency from 1 (A1 AF = 1-A2 AF). For example, the SNP rs1874633 has the following case and control allele frequencies: case A1 (A) = 0.514; case A2 (G) = 0.486; control A1 (A) = 0.449; and control A2 (G) = 0.551, where the nucleotide is provided in paranthesis. SNPs with blank allele frequencies were untyped.

Table 22

dbSNP rs#	Position in Figure 4	Chromosome Position	A1/A2 Allele	A2 Case AF	A2 Control AF	p-Value
1874633	196	68275196	A/G	0.486	0.551	0.0292
1846060	13311	68288311	G/A	0.416	0.468	0.0792
451352	14486	68289486	C/T	0.474	0.411	0.0365
355468	14691	68289691	A/T	0.839	0.839	0.9913
355469	15551	68290551	C/G	0.089	0.072	0.3028
355470	17702	68292702	T/C	0.077	0.059	0.2261
355471	17872	68292872	T/C	0.476	0.442	0.2613
191650	19588	68294588	T/C	0.122	0.103	0.3282
355472	19910	68294910	T/A	0.491	0.568	0.0114
1874635	20006	68295006	A/C	0.206	0.238	0.2083
1497430	20575	68295575	A/G	0.389	0.476	0.0039
2254659	21092	68296092	G/A	0.554	0.587	0.2664
3822197	22830	68297830	C/T	0.028	0.018	0.2999
2632453	23455	68298455	A/G	0.866	0.895	0.1407
2646282	23716	68298716	G/A	0.137	0.090	0.0146
2646285	23890	68298890	T/G	0.400	0.335	0.0269
768244	24001	68299001	C/T	0.299	0.286	0.6333
724199	24995	68299995	G/A	0.446	0.374	0.0150
1187960	27282	68302282	T/C	0.071	0.060	0.4859
1187961	27779	68302779	C/T	0.499	0.549	0.0968
355518	29099	68304099	C/G	0.432	0.491	0.0473
355519	31185	68306185	A/G	0.095	0.076	0.2836
355511	33994	68308994	C/T	0.450	0.361	0.0030
451397	34942	68309942	T/C	0.442	0.512	0.0210
355513	35137	68310137	C/G	0.385	0.334	0.0748
355514	36538	68311538	T/C	0.423	0.479	0.0596
355515	37139	68312139	C/T	0.422	0.362	0.0395
1056789	37358	68312358	G/A	0.494	0.539	0.1409
2646290	38828	68313828	A/G	0.393	0.337	0.0559
190255	39469	68314469	T/C	0.459	0.514	0.0664
355466	40233	68315233	T/C	0.404	0.468	0.0328
355465	40472	68315472	A/T	0.481	0.547	0.0281
2646292	41679	68316679	C/T	0.422	0.370	0.0820
2632454	41682	68316682	G/A	0.914	0.936	0.1705
1056787	42831	68317831	A/G	0.909	0.860	0.0112
CENPC1 SNP1	42976	68317976	A/G	0.367	0.306	0.0322
173317	44128	68319128	A/G	0.087	0.080	0.6745
451344	44195	68319195	C/T	0.366	0.307	0.0392
355510	46769	68321769	G/A	0.487	0.514	0.3645
355508	47363	68322363	G/C	0.086	0.070	0.3357
451391	48843	68323843	C/T	0.440	0.370	0.0171
355500	52574	68327574	A/G	0.874	0.904	0.1103
355499	52602	68327602	A/G	0.874	0.884	0.5959
355498	53212	68328212	A/G	0.477	0.528	0.0932

dbSNP rs#	Position in Figure 4	Chromosome Position	A1/A2 Allele	A2 Case AF	A2 Control AF	p-Value
1187974	53781	68328781	C/G	0.563	0.540	0.4558
355493	54710	68329710	A/T	0.950	0.932	0.2013
2632456	55808	68330808	G/A	0.091	0.074	0.3234
1825790	57987	68332987	T/A	0.043	0.067	0.0709
355475	58556	68333556	C/A	0.252	0.199	0.0343
1391110	59148	68334148	T/A	0.696	0.679	0.5418
1442557	59286	68334286	G/C	0.458	0.523	0.0306
355478	60217	68335217	A/G	0.314	0.371	0.0474
189579	60412	68335412	G/T	0.008	0.002	0.1543
355480	60753	68335753	C/T	0.905	0.910	0.7624
355481	60791	68335791	T/G	0.974	0.979	0.5823
355483	61524	68336524	A/G	0.371	0.414	0.1461
355485	62543	68337543	T/C	0.487	0.541	0.0732
2646267	62825	68337825	A/G	0.368	0.312	0.0520
2646268	62826	68337826	A/C	0.306	0.239	0.0123
355486	62857	68337857	C/T	0.438	0.375	0.0316
355487	63400	68338400	T/C	0.468	0.559	0.0031
355488	63960	68338960	T/A	0.533	0.454	0.0090
355489	64307	68339307	A/G	0.367	0.324	0.1291
451376	64539	68339539	A/G	0.873	0.871	0.9287
1353626	65728	68340728	A/G	0.356	0.383	0.3657
2632450	66000	68341000	G/A	0.256	0.259	0.9210
2646269	66521	68341521	T/G	0.084	0.062	0.1648
2276945	68185	68343185	C/T	0.459	0.510	0.0866
3775861	69643	68344643	G/A	0.532	0.521	0.7150
1403151	74909	68349909	C/A	0.739	0.801	0.0148
1843833	82973	68357973	T/G	0.920	0.939	0.2355
1843831	83039	68358039	T/C	0.032	0.040	0.5196
3806810	85713	68360713	A/G	0.078	0.058	0.1942
3775862	86873	68361873	T/C	0.744	0.765	0.4224
1962700	90293	68365293	T/G	0.733	0.739	0.8308
2046601	91810	68366810	T/G	0.080	0.073	0.6571
2171386	92609	68367609	A/G	0.685	0.662	0.4056
2046599	92884	68367884	G/A	0.717	0.755	0.1540
355490			A/T	0.495	0.548	0.0763

[0269] Figure 16 shows the proximal SNPs in and around the *ICAM* region for females. The position of each SNP on the chromosome is presented on the x-axis. The y-axis gives the negative logarithm (base 10) of the p-value comparing the estimated allele in the case group to that of the control group. The minor allele frequency of the control group for each SNP designated by an X or other symbol on the graphs in Figure 16 can be determined by consulting Table 22. By proceeding down the Table from top to bottom and across the graphs from left to right the allele frequency associated with each symbol shown can be determined.

[0270] To aid the interpretation, multiple lines have been added to the graph. The broken horizontal lines are drawn at two common significance levels, 0.05 and 0.01. The vertical broken lines are drawn every 20kb to assist in the interpretation of distances between SNPs. Two other lines are drawn to expose linear trends in the association of SNPs to the disease. The light gray line (or generally bottom-most curve) is a nonlinear smoother through the data points on the graph using a local polynomial regression method (W.S. Cleveland, E. Grosse and W.M. Shyu (1992) Local regression models. Chapter 8 of Statistical Models in S eds J.M. Chambers and T.J. Hastie,

Wadsworth & Brooks/Cole.). The black line (or generally top-most curve, *e.g.*, see peak in left-most graph just to the left of position 92150000) provides a local test for excess statistical significance to identify regions of association. This was created by use of a 10kb sliding window with 1kb step sizes. Within each window, a chi-square goodness of fit test was applied to compare the proportion of SNPs that were significant at a test wise level of 0.01, to the proportion that would be expected by chance alone (0.05 for the methods used here). Resulting p-values that were less than 10^{-8} were truncated at that value.

[0271] Finally, the gene or genes present in the loci region of the proximal SNPs as annotated by Locus Link ([http address: www.ncbi.nlm.nih.gov/LocusLink/](http://www.ncbi.nlm.nih.gov/LocusLink/)) are provided on the graph. The exons and introns of the genes in the covered region are plotted below each graph at the appropriate chromosomal positions. The gene boundary is indicated by the broken horizontal line. The exon positions are shown as thick, unbroken bars. An arrow is placed at the 3' end of each gene to show the direction of transcription.

Additional Genotyping

[0272] In addition to the CENCP1 incident SNP, another SNP (rs1056787) was genotyped in the discovery cohort and found to be significantly associated with breast cancer with a p-value of 0.0266. See Table 25.

[0273] The methods used to verify and genotype the proximal SNP of Table 15 are the same methods described in Examples 1 and 2 herein. The PCR primers and extend primers used in these assays are provided in Table 11 and Table 12, respectively.

Table 23

dbSNP rs#	Second PCR primer	First PCR primer
1056787	ACGTTGGATGCATTTTCATATTTGTAGATC	ACGTTGGATGTCTCAGCCCTCTGATAAAAC

Table 24

dbSNP rs#	Extend Primer	Term Mix
1056787	GGATACAAGTTATGCTTTGATAG	ACT

[0274] Table 13, below, shows the case and control allele frequencies along with the p-values for the SNPs genotyped. The disease associated allele of column 4 is in bold and the disease associated amino acid of column 5 is also in bold. The chromosome position provided corresponds to NCBI's Build 33.

Table 25: Genotyping Results

dbSNP rs#	Position in Figure 4	Chromo- some Position	Alleles (A1/A2)	Amino Acid Change	AF F case	AF F control	p-value	Odds Ratio
1056787	42831	68317831	A/G	D389G	A = 0.030 G = 0.970	A = 0.110 G = 0.890	0.0266	1.640

Example 7*In Vitro* Production of Target Polypeptides

[0275] cDNA is cloned into a pIVEX 2.3-MCS vector (Roche Biochem) using a directional cloning method. A cDNA insert is prepared using PCR with forward and reverse primers having 5' restriction site tags (in frame) and 5-6 additional nucleotides in addition to 3' gene-specific portions, the latter of which is typically about twenty to about twenty-five base pairs in length. A Sal I restriction site is introduced by the forward primer and a Sma I restriction site is introduced by the reverse primer. The ends of PCR products are cut with the corresponding restriction enzymes (*i.e.*, Sal I and Sma I) and the products are gel-purified. The pIVEX 2.3-MCS vector is linearized using the same restriction enzymes, and the fragment with the correct sized fragment is isolated by gel-purification. Purified PCR product is ligated into the linearized pIVEX 2.3-MCS vector and *E. coli* cells transformed for plasmid amplification. The newly constructed expression vector is verified by restriction mapping and used for protein production.

[0276] *E. coli* lysate is reconstituted with 0.25 ml of Reconstitution Buffer, the Reaction Mix is reconstituted with 0.8 ml of Reconstitution Buffer; the Feeding Mix is reconstituted with 10.5 ml of Reconstitution Buffer; and the Energy Mix is reconstituted with 0.6 ml of Reconstitution Buffer. 0.5 ml of the Energy Mix was added to the Feeding Mix to obtain the Feeding Solution. 0.75 ml of Reaction Mix, 50 μ l of Energy Mix, and 10 μ g of the template DNA is added to the *E. coli* lysate.

[0277] Using the reaction device (Roche Biochem), 1 ml of the Reaction Solution is loaded into the reaction compartment. The reaction device is turned upside-down and 10 ml of the Feeding Solution is loaded into the feeding compartment. All lids are closed and the reaction device is loaded into the RTS500 instrument. The instrument is run at 30°C for 24 hours with a stir bar speed of 150 rpm. The pIVEX 2.3 MCS vector includes a nucleotide sequence that encodes six consecutive histidine amino acids on the C-terminal end of the target polypeptide for the purpose of protein purification. Target polypeptide is purified by contacting the contents of reaction device with resin modified with Ni²⁺ ions. Target polypeptide is eluted from the resin with a solution containing free Ni²⁺ ions.

Example 8

Cellular Production of Target Polypeptides

[0278] Nucleic acids are cloned into DNA plasmids having phage recombination sites and target polypeptides are expressed therefrom in a variety of host cells. Alpha phage genomic DNA contains short sequences known as attP sites, and *E. coli* genomic DNA contains unique, short sequences known as attB sites. These regions share homology, allowing for integration of phage DNA into *E. coli* via directional, site-specific recombination using the phage protein Int and the *E. coli* protein IHF. Integration produces two new att sites, L and R, which flank the inserted prophage DNA. Phage excision from *E. coli* genomic DNA can also be accomplished using these two proteins with the addition of a second phage protein, Xis. DNA vectors have been produced where the integration/excision process is modified to allow for the directional integration or excision of a target DNA fragment into a backbone vector in a rapid *in vitro* reaction (Gateway™ Technology (Invitrogen, Inc.)).

[0279] A first step is to transfer the nucleic acid insert into a shuttle vector that contains attL sites surrounding the negative selection gene, ccdB (*e.g.* pENTER vector, Invitrogen, Inc.). This transfer process is accomplished by digesting the nucleic acid from a DNA vector used for sequencing, and to ligate it into the multicloning site of the shuttle vector, which will place it between the two attL sites while removing the negative selection gene ccdB. A second method is to amplify the nucleic acid by the polymerase chain reaction (PCR) with primers containing attB sites. The amplified fragment then is integrated into the shuttle vector using Int and IHF. A third method is to utilize a topoisomerase-mediated process, in which the nucleic acid is amplified via PCR using gene-specific primers with the 5' upstream primer containing an additional CACC sequence (*e.g.*, TOPO® expression kit (Invitrogen, Inc.)). In conjunction with Topoisomerase I, the PCR amplified fragment can be cloned into the shuttle vector via the attL sites in the correct orientation.

[0280] Once the nucleic acid is transferred into the shuttle vector, it can be cloned into an expression vector having attR sites. Several vectors containing attR sites for expression of target polypeptide as a native polypeptide, N-fusion polypeptide, and C-fusion polypeptides are commercially available (*e.g.*, pDEST (Invitrogen, Inc.)), and any vector can be converted into an expression vector for receiving a nucleic acid from the shuttle vector by introducing an insert having an attR site flanked by an antibiotic resistant gene for selection using the standard methods described above. Transfer of the nucleic acid from the shuttle vector is accomplished by directional recombination using Int, IHF, and Xis (LR clonase). Then the desired sequence can be transferred to an expression vector by carrying out a one hour incubation at room temperature with Int, IHF, and Xis, a ten minute incubation at 37°C with proteinase K, transforming bacteria and allowing expression for one hour, and then plating on selective media. Generally, 90% cloning efficiency is achieved by this method. Examples of expression vectors are pDEST 14 bacterial expression vector with att7

promoter, pDEST 15 bacterial expression vector with a T7 promoter and a N-terminal GST tag, pDEST 17 bacterial vector with a T7 promoter and a N-terminal polyhistidine affinity tag, and pDEST 12.2 mammalian expression vector with a CMV promoter and neo resistance gene. These expression vectors or others like them are transformed or transfected into cells for expression of the target polypeptide or polypeptide variants. These expression vectors are often transfected, for example, into murine-transformed adipocyte cell line 3T3-L1, (ATCC), human embryonic kidney cell line 293, and rat cardiomyocyte cell line H9C2.

Example 9

Haplotype analysis of the *KIAA0783* locus

[0281] Markers rs1681290, rs220097, rs3801435, and rs2883140 are significantly associated with breast cancer at the allele and genotype levels ($P < 0.05$). Strong LD is observed between markers 1681290, 220097, 3801435, and 2883140 ($r^2 > 0.90$). Pearson chi-squared statistics indicate that haplotypes are significantly associated with breast cancer. Haplotypes TTGCGG, CTGCGG, and TCATAT contribute most to the aggregate test statistic. Odds ratios and score tests indicate that individuals with the TTGCGG and CTGCGG haplotypes are significantly less likely to have breast cancer, while individuals with the TCATAT haplotype are slightly more likely to be affected than individuals with other haplotypes.

Statistics

[0282] Chi-squared statistics are estimated to assess whether 1) alleles and genotypes are associated with breast cancer status and 2) marker genotype frequencies deviate significantly from Hardy-Weinberg equilibrium (HWE). Haplotype frequencies and relative frequencies are estimated, as well as several statistics (r^2 , D' , and p-value) that gauge the extent and stability of linkage disequilibrium between markers in each region. Chi-squared statistics and score tests are estimated to determine whether reconstructed haplotypes are significantly associated with breast cancer status ($P < 0.05$). P-values are estimated for 1) the full set of reconstructed haplotypes and 2) a reduced set that excludes haplotypes with observed frequencies less than 10. Results are presented by chromosome order.

ResultsSummary Statistics: Alleles and Genotypes**SNP Locations**

SNP.ID	Type	Location
218981	Proximal	10720511
1681284	Proximal	10739011
1681290	Proximal	10741656
220097	Incident	10759860
3801435	Proximal	10771563
2883140	Proximal	10806368

Allele by GYNGroup

	N	Case (N=510)	Control (N=538)	Test Statistic
218981:T	1028	47%(232)	45%(239)	Chi-square=0.68 d.f.=1 P=0.41
1681284:C	1032	56%(276)	50%(267)	Chi-square=3.51 d.f.=1 P=0.0608
1681290:A	1018	72%(352)	63%(330)	Chi-square=8.92 d.f.=1 P=0.00282
220097:C	996	29%(139)	38%(196)	Chi-square=8.03 d.f.=1 P=0.00461
3801435:G	1018	28%(138)	38%(200)	Chi-square=9.69 d.f.=1 P=0.00185
2883140:T	1012	73%(351)	62%(330)	Chi-square=12.78 d.f.=1 P<0.001

Genotype by GYNGroup

	N	Case (N=255)	Control (N=269)	Test Statistic
218981:CC	514	27%(67)	27%(73)	Chi-square=2.41 d.f.=2 P=0.299
CT		51%(126)	56%(151)	
TT		22%(53)	16%(44)	
1681284:TT	516	19%(48)	26%(70)	Chi-square=3.77 d.f.=2 P=0.152
TC		50%(124)	48%(129)	
CC		31%(76)	26%(69)	
1681290:GG	509	9%(21)	16%(41)	Chi-square=8.64 d.f.=2 P=0.0133

	N	Case (N=255)	Control (N=269)	Test Statistic
GA		40%(98)	43%(114)	
AA		52%(127)	41%(108)	
220097:TT	498	50%(119)	40%(104)	Chi-square=8.06 d.f.=2 P=0.0177
TC		42%(99)	45%(116)	
CC		8%(20)	15%(40)	
3801435:AA	509	51%(124)	40%(107)	Chi-square=9.78 d.f.=2 P=0.0075
AG		41%(100)	44%(118)	
GG		8%(19)	15%(41)	
2883140:GG	506	8%(19)	16%(42)	Chi-square=12.14 d.f.=2 P=0.00231
GT		39%(93)	44%(116)	
TT		54%(129)	40%(107)	

Genotype QC: Test of Hardy-Weinberg Proportions

All

	A.freq	D	ChiSq	Pvalue
218981	0.543	-0.01990	3.290	0.0697
1681284	0.526	0.00564	0.263	0.6080
1681290	0.670	0.01170	1.430	0.2320
220097	0.664	0.00584	.351	.5530
3801435	0.667	0.00585	.355	.5510
2883140	0.675	.01360	.970	.1610

Control

	A.freq	D	ChiSq	Pvalue
218981	0.554	-0.03380	5.010	0.0252
1681284	0.502	0.01030	0.453	0.5010
1681290	0.627	0.01470	1.050	0.3050
220097	0.620	0.00904	0.393	0.5310
3801435	0.624	0.01190	0.684	0.4080
2883140	0.625	0.01700	1.410	0.2350

Summary Statistics: Linkage Disequilibrium**PHASE Haplotype Frequencies**

	H.freq	H.relfreq
CCATAT	91	0.089
CCGCGG	4	0.004
CTACGG	5	0.005
CTACGT	1	0.001
CTATAT	142	0.138
CTGCAG	1	0.001
CTGCAT	2	0.002
CTGCGG	300	0.292
CTGCGT	10	0.010
CTGTAT	1	0.001
TCACGG	1	0.001
TCATAG	1	0.001
TCATAT	443	0.432
TTATAT	3	0.003
TTGCGG	21	0.020

Linkage Disequilibrium Between Markers r^2

x	218981	1681284	1681290	220097	3801435	2883140
218981	1.000	0.603	0.311	0.316	0.311	0.292
1681284	0.603	1.000	0.524	0.532	0.525	0.498
1681290	0.311	0.524	1.000	0.965	0.952	0.914
220097	0.316	0.532	0.965	1.000	0.987	0.940
3801435	0.311	0.525	0.952	0.987	1.000	0.944
2883140	0.292	0.498	0.914	0.940	0.944	1.000

D'

	218981	1681284	1681290	220097	3801435	2883140
218981	1.000	0.803	0.728	0.725	0.724	0.715
1681284	0.803	1.000	0.978	0.972	0.972	0.966
1681290	0.728	0.978	1.000	0.996	0.982	0.969
220097	0.725	0.972	0.996	1.000	1.000	0.995
3801435	0.724	0.972	0.982	1.000	1.000	0.991
2883140	0.715	0.966	0.969	0.995	0.991	1.000

P-value

	218981	1681284	1681290	220097	3801435	2883140
218981	1	0	0	0	0	0
1681284	0	1	0	0	0	0
1681290	0	0	1	0	0	0
220097	0	0	0	1	0	0
3801435	0	0	0	0	1	0
2883140	0	0	0	0	0	1

Haplotype by GYNGroup**All Haplotypes**

	Case	Case(%)	Case.X²	Control	Control(%)	Control.X²	OR	ln.OR
CTGCAG	0	0.00	0.48	1	0.10	0.44	0.0000	-Inf
TCACGG	0	0.00	0.48	1	0.10	0.44	-Inf	
						0.0000		
TCATAG	0	0.00	0.48	1	0.10	0.44	0.0000	-Inf
TTATAT	0	0.00	1.44	3	0.29	1.33	0.0000	-Inf
TTGCGG	1	0.10	8.17	20	1.95	7.53	0.0491	-3.0139
CCGCGG	1	0.10	0.44	3	0.29	0.40	0.3327	-1.1005
CTACGG	2	0.19	0.07	3	0.29	0.06	0.6660	-0.4065
CTGCGG	129	12.57	1.53	171	16.67	1.41	0.7191	-0.3298
CCATAT	43	4.19	0.01	48	4.68	0.01	0.8913	-0.1151

	Case	Case(%)	Case.X ²	Control	Control(%)	Control.X ²	OR	ln. OR
CTGCAT	1	0.10	0.00	1	0.10	0.00	1.0000	0.0000
TCATAT	230	22.42	1.45	213	20.76	1.34	1.1029	0.0979
CTATAT	76	7.41	0.92	66	6.43	0.85	1.1636	0.1515
CTGCGT	7	0.68	1.01	3	0.29	0.93	2.3425	0.8512
CTACGT	1	0.10	0.56	0	0.00	0.52	Inf	Inf
CTGTAT	1	0.10	0.56	0	0.00	0.52	Inf	Inf

Pearson Chi-squared Test = 33.8392, DF = 14, P-value = 0.002177

Permutation Test P-value = 0.01

PHASE Haplotypes (Low Frequency Excluded)

	Case	Case(%)	Case.X ²	Control	Control(%)	Control.X ²	OR	ln. OR
TTGCGG	1	0.10	8.23	20	1.99	7.68	0.0491	- 3.0139
CTGCGG	129	12.81	1.72	171	16.98	1.61	0.7183	- 0.3309
CCATAT	43	4.27	0.02	48	4.77	0.02	0.8912	- 0.1152
TCATAT	230	22.84	1.23	213	21.15	1.14	1.1034	0.0984
CTATAT	76	7.55	0.81	66	6.55	0.76	1.1639	0.1518
CTGCGT	7	0.70	0.98	3	0.30	0.91	2.3427	0.8513

Pearson Chi-squared Test = 25.1157, DF = 5, P-value = 0.0001323

haplo.score Haplotypes

	Hap.Freq	Score	P. X ²	P.Sim
TTGCGG	0.0203	-3.7664	0.0002	0.0001
TTATAT	0.0063	-2.5040	0.0123	0.0097
CTGCGG	0.2947	-2.0103	0.0444	0.0438
CCATAT	0.0902	-0.3982	0.6905	0.7174
CTATAT	0.1318	1.4254	0.1540	0.1538
CTGCGT	0.0084	1.5778	0.1146	0.1243
TCATAT	0.4342	2.3889	0.0169	0.0180

Global Score = 27.2432, DF = 7, Global P.X² = 3e-04, Global P.Sim = 1e-04

Example 10Haplotype analysis of the *CENPCI* locus

[0283] Each SNP noted below is significantly associated with breast cancer at allele level ($P < 0.05$). rs355510 maintains a significant relationship with disease at the genotype level. Near-complete LD is observed across the entire region. Pearson chi-squared statistics demonstrate that haplotypes CCAC and TTGT are significantly associated with breast cancer after low frequency haplotypes are removed from the analysis. Odds ratios and score tests indicate that individuals with the CCAC haplotype are significantly less likely to have breast cancer, while individuals with the TTGT haplotype are at moderately increased risk for disease vs. individuals with other haplotypes.

Statistics

[0284] Chi-squared statistics are estimated to assess whether 1) alleles and genotypes are associated with breast cancer status and 2) marker genotype frequencies deviate significantly from Hardy-Weinberg equilibrium (HWE). Haplotype frequencies and relative frequencies are estimated, as well as several statistics (r^2 , D' , and p-value) that gauge the extent and stability of linkage disequilibrium between markers in each region. Chi-squared statistics and score tests are estimated to determine whether reconstructed haplotypes are significantly associated with breast cancer status ($P < 0.05$). P-values are estimated for 1) the full set of reconstructed haplotypes and 2) a reduced set that excludes haplotypes with observed frequencies less than 10. Results are presented by chromosome order.

ResultsSummary Statistics: Alleles and Genotypes**SNP Locations**

SNP.ID	Type	Location
GP04.071927035	Proximal	68289486
355511	Proximal	68308994
355510	Incident	68321769
355487	Proximal	68338400

Allele by GYNGroup

	N	Case (N=508)	Control (N=536)	Test Statistic
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Genotype by GYNGroup

	N	Case (N=254)	Control (N=268)	Test Statistic
GP04.071927035:CC	511	28%(69)	37%(98)	Chi-square=5.33 d.f.=2 P=0.0695
CT		52%(127)	48%(129)	
TT		20%(49)	15%(39)	
355511:TT	505	20%(48)	14%(38)	Chi-square=4.47 d.f.=2 P=0.107
TC		51%(124)	49%(129)	
CC		29%(70)	37%(96)	
355510:GG	502	20%(49)	15%(38)	Chi-square=6.52 d.f.=2 P=0.0383
GA		52%(125)	47%(123)	
AA		28%(68)	38%(99)	
355487:TT	496	20%(48)	15%(37)	Chi-square=5.35 d.f.=2 P=0.069
TC		52%(126)	48%(123)	
CC		28%(68)	37%(94)	

Genotype QC: Test of Hardy-Weinberg Proportions**All**

	A.freq	D	ChiSq	Pvalue
GP04.071927035	0.577	-0.00599	0.303	0.582
355511	0.579	-0.00630	0.337	0.562
355510	0.577	-0.00599	0.303	0.582
355487	0.577	-0.00599	0.303	0.582

Control

	A.freq	D	ChiSq	Pvalue
GP04.071927035	0.609	-0.00420	0.0814	0.775
355511	0.611-0.00653	0.1970	0.657	
355510	0.609	-0.00420	0.0814	0.775
355487	0.611	-0.00271	0.0340	0.854

Summary Statistics: Linkage Disequilibrium**PHASE Haplotype Frequencies**

	H.freq	H.relfreq
CCAC	581	0.576
CCAT	1	0.001
TCGT	2	0.002
TTGC	1	0.001
TTGT	423	0.420

Linkage Disequilibrium Between Markers**r²**

	GP04.071927035	355511	355510	355487
GP04.071927035	1.000	0.992	1.000	0.992
355511	0.992	1.000	0.992	0.984
355510	1.000	0.992	1.000	0.992
355487	0.992	0.984	0.992	1.000

D'

	GP04.071927035	355511	355510	355487
GP04.071927035	1.000	1.000	1.000	0.996
355511	1.000	1.000	1.000	0.996
355510	1.000	1.000	1.000	0.996
355487	0.996	0.996	0.996	1.000

P-value

	GP04.071927035	355511	355510	355487
GP04.071927035	1	0	0	0
355511	0	1	0	0

355510	0	0	1	0
355487	0	0	0	1

Haplotype by GYNGroup**PHASE Haplotypes (All)**

	Case	Case(%)	Case.X ²	Control	Control(%)	Control.X ²	OR	ln.OR
TTGC	0	0.00	0.48	1	0.10	0.44	0.0000	-Inf
CCAC	262	25.99	1.03	319	31.65	0.95	0.7586	-0.2763
TCGT	1	0.10	0.00	1	0.10	0.00	1.0000	0.0000
TTGT	220	21.83	1.41	203	20.14	1.30	1.1071	0.1017
CCAT	1	0.10	0.56	0	0.00	0.52	Inf	Inf

Pearson Chi-squared Test = 6.6985, DF = 4, P-value = 0.1527

Permutation Test P-value = 0.56

PHASE Haplotypes (Low Frequency Excluded)

	Case	Case(%)	Case.X ²	Control	Control(%)	Control.X ²	OR	ln.OR
CCAC	262	26.10	1.03	319	31.77	0.95	0.7582	-0.2768
TTGT	220	21.91	1.41	203	20.22	1.30	1.1072	0.1018

Pearson Chi-squared Test = 4.4162, DF = 1, P-value = 0.0356

haplo.score Haplotypes

	Hap.Freq	Score	P.X ²	P.Sim
CCAC	0.5772	-2.3513	0.0187	0.0168
TTGT	0.4208	2.2111	0.0270	0.0249

Global Score = 7.5085, DF = 2, Global P.X² = 0.0234, Global P.Sim = 0.0117

[0285] Citation of the above publications or documents is not intended as an admission that any of the foregoing is pertinent prior art, nor does it constitute any admission as to the contents or date of these publications or documents. U.S. patents and other publications referenced herein are hereby incorporated by reference.

[0286] Modifications may be made to the foregoing without departing from the basic aspects of the invention. Although the invention has been described in substantial detail with reference to one or more specific embodiments, those of skill in the art will recognize that changes may be made to the embodiments specifically disclosed in this application, yet these modifications and improvements are within the scope and spirit of the invention, as set forth in the claims which follow. All publications or patent documents cited in this specification are incorporated herein by reference as if each such publication or document was specifically and individually indicated to be incorporated herein by reference.

What is claimed is:

1. A method for identifying a subject at risk of breast cancer, which comprises detecting the presence or absence of one or more polymorphic variations associated with breast cancer in a nucleic acid sample from a subject, wherein the one or more polymorphic variations are detected in a nucleotide sequence selected from the group consisting of:

- (a) a nucleotide sequence in SEQ ID NO: 1-4;
- (b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-4;
- (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-4;
- (d) a fragment of a nucleotide sequence of (a), (b), or (c);

whereby the presence of the polymorphic variation is indicative of the subject being at risk of breast cancer.

2. The method of claim 1, which further comprises obtaining the nucleic acid sample from the subject.

3. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 1 selected from the group consisting of 133, 7938, 8873, 13221, 17288, 25732, 26923, 39977, 41284, 41410, 41477, 41514, 42606, 42742, 59515, 59808, 60265, 67152, 68332, 71128 and 76427.

4. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 1 selected from the group consisting of 7938, 26923, 39977 and 59808.

5. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in a region spanning positions 7938-59808 in SEQ ID NO: 1.

6. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 2 selected from the group consisting of 201, 6395, 8558, 9429, 9809, 10072, 10511, 11556, 16857, 16951, 17027, 17177, 17615, 17950, 18329, 18384, 18561, 18579, 18871, 27152, 27306, 28091, 28661, 29011, 29962, 29969, 30085, 31656, 31685, 31749, 45389, 45459, 46647, 49860, 53061, 57308, 61563, 61660, 62212, 67090, 67198, 70071, 70191, 74006, 75600, 85761, 90798, 90883, 91259, 95416, 95446, 96368, 97050, 97362, 97630, 97989 and 98107.

7. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 2 selected from the group consisting of 10511, 11556, 17177, 18384, 28661, 31656, 31685, 31749, 45389, 45459, 46647, 49860, 53061, 57308, 61563, 61660, 67090, 67198, 70071, 74006, 75600, 85761, 90798, 90883, 91259, 95416, 95446, 96368, 97362, 97630, 97989 and 98107.
8. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in a region spanning positions 10511-98107 in SEQ ID NO: 2.
9. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 3 selected from the group consisting of 160, 6053, 9719, 10481, 10676, 17179, 18561, 18658, 18694, 18858, 24582, 24683, 24767, 27402, 28150, 28494, 32003, 35588, 35619, 35856, 36254, 37314, 40033, 40095, 42593, 42799, 43090, 46683, 49774, 51796, 52079, 53857, 53971, 55899, 60682, 61291, 72720, 72752, 85507 and 89751.
10. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 3 selected from the group consisting of 160, 6053, 18658, 18694, 18858, 24683, 27402, 28494, 32003, 35588, 35856, 40095, 46683, 52079, 53857, 72720 and 72752.
11. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in a region spanning positions 160-72752 in SEQ ID NO: 3.
12. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 4 selected from the group consisting of 196, 13311, 14486, 14691, 15551, 17702, 17872, 19588, 19910, 20006, 20575, 21092, 22830, 23455, 23716, 23890, 24001, 24995, 27282, 27779, 29099, 31185, 33994, 34942, 35137, 36538, 37139, 37358, 38828, 39469, 40233, 40472, 41679, 41682, 42831, 42976, 44128, 44195, 46769, 47363, 48843, 52574, 52602, 53212, 53781, 54710, 55808, 57987, 58556, 59148, 59286, 60217, 60412, 60753, 60791, 61524, 62543, 62825, 62826, 62857, 63400, 63960, 64307, 64539, 65728, 66000, 66521, 68185, 69643, 74909, 82973, 83039, 85713, 86873, 90293, 91810, 92609, 92884 and 42831.
13. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 4 selected from the group consisting of 196, 13311, 14486, 19910, 20575, 23716, 23890, 24995, 29099, 33994, 34942, 37139, 40233, 40472, 42831, 42976, 44195, 48843, 58556, 59286, 60217, 62826, 62857, 63400, 63960 and 74909.

14. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in a region spanning positions 196-74909 in SEQ ID NO: 4.

15. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in linkage disequilibrium with one or more positions in claim 3, 6, 9 or 12.

16. The method of claim 1, wherein detecting the presence or absence of the one or more polymorphic variations comprises:

hybridizing an oligonucleotide to the nucleic acid sample, wherein the oligonucleotide is complementary to a nucleotide sequence in the nucleic acid and hybridizes to a region adjacent to the polymorphic variation;

extending the oligonucleotide in the presence of one or more nucleotides, yielding extension products; and

detecting the presence or absence of a polymorphic variation in the extension products.

17. The method of claim 1, wherein the subject is a human.

18. A method for identifying a polymorphic variation associated with breast cancer proximal to an incident polymorphic variation associated with breast cancer, which comprises:

identifying a polymorphic variation proximal to the incident polymorphic variation associated with breast cancer, wherein the polymorphic variation is detected in a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence in SEQ ID NO: 1-4;

(b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-4;

(c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-4;

(d) a fragment of a nucleotide sequence of (a), (b), or (c) comprising the polymorphic variation;

determining the presence or absence of an association of the proximal polymorphic variant with breast cancer.

19. The method of claim 18, wherein the incident polymorphic variation is at a position in claim 3, 6, 9 or 12.

20. The method of claim 18, wherein the proximal polymorphic variation is within a region between about 5 kb 5' of the incident polymorphic variation and about 5 kb 3' of the incident polymorphic variation.

21. The method of claim 18, which further comprises determining whether the proximal polymorphic variation is in linkage disequilibrium with the incident polymorphic variation.

22. The method of claim 18, which further comprises identifying a second polymorphic variation proximal to the identified proximal polymorphic variation associated with breast cancer and determining if the second proximal polymorphic variation is associated with breast cancer.

23. The method of claim 22, wherein the second proximal polymorphic variant is within a region between about 5 kb 5' of the incident polymorphic variation and about 5 kb 3' of the proximal polymorphic variation associated with breast cancer.

24. An isolated nucleic acid comprising a nucleotide sequence selected from the group consisting of:

- (a) a nucleotide sequence in SEQ ID NO: 1-4;
- (b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-4;
- (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-4;
- (d) a fragment of a nucleotide sequence of (a), (b), or (c); and
- (e) a nucleotide sequence complementary to the nucleotide sequences of (a), (b), (c), or (d);

wherein the nucleotide sequence comprises one or more polymorphic variants associated with breast cancer selected from the group consisting of a thymine at position 7938 in SEQ ID NO: 1, a cytosine at position 26923 in SEQ ID NO: 1, a thymine at position 39977 in SEQ ID NO: 1, a thymine at position 59808 in SEQ ID NO: 1, a thymine at position 10511 in SEQ ID NO: 2, a cytosine at position 11556 in SEQ ID NO: 2, a thymine at position 17177 in SEQ ID NO: 2, a thymine at position 18384 in SEQ ID NO: 2, an adenine at position 28661 in SEQ ID NO: 2, an adenine at position 31656 in SEQ ID NO: 2, an adenine at position 31685 in SEQ ID NO: 2, a guanine at position 31749 in SEQ ID NO: 2, a thymine at position 45389 in SEQ ID NO: 2, a guanine at position 45459 in SEQ ID NO: 2, an adenine at position 46647 in SEQ ID NO: 2, a thymine at position 49860 in SEQ ID NO: 2, a thymine at position 53061 in SEQ ID NO: 2, an adenine at position 57308 in SEQ ID NO: 2, a guanine at position 61563 in SEQ ID NO: 2, a guanine at position 61660 in SEQ ID NO: 2, a guanine at position 67090 in SEQ ID NO: 2, a cytosine at position 67198

in SEQ ID NO: 2, an adenine at position 70071 in SEQ ID NO: 2, a cytosine at position 74006 in SEQ ID NO: 2, an adenine at position 75600 in SEQ ID NO: 2, a guanine at position 85761 in SEQ ID NO: 2, a thymine at position 90798 in SEQ ID NO: 2, a cytosine at position 90883 in SEQ ID NO: 2, an adenine at position 91259 in SEQ ID NO: 2, a cytosine at position 95416 in SEQ ID NO: 2, a thymine at position 95446 in SEQ ID NO: 2, a thymine at position 96368 in SEQ ID NO: 2, a thymine at position 97362 in SEQ ID NO: 2, an adenine at position 97630 in SEQ ID NO: 2, a cytosine at position 97989 in SEQ ID NO: 2, a thymine at position 98107 in SEQ ID NO: 2, an adenine at position 160 in SEQ ID NO: 3, a guanine at position 6053 in SEQ ID NO: 3, a guanine at position 18658 in SEQ ID NO: 3, a guanine at position 18694 in SEQ ID NO: 3, a thymine at position 18858 in SEQ ID NO: 3, a guanine at position 24683 in SEQ ID NO: 3, a guanine at position 27402 in SEQ ID NO: 3, a thymine at position 28494 in SEQ ID NO: 3, an adenine at position 32003 in SEQ ID NO: 3, a cytosine at position 35588 in SEQ ID NO: 3, an adenine at position 35856 in SEQ ID NO: 3, a guanine at position 40095 in SEQ ID NO: 3, an adenine at position 46683 in SEQ ID NO: 3, an adenine at position 52079 in SEQ ID NO: 3, a cytosine at position 53857 in SEQ ID NO: 3, an adenine at position 72720 in SEQ ID NO: 3, a cytosine at position 72752 in SEQ ID NO: 3, an adenine at position 196 in SEQ ID NO: 4, a guanine at position 13311 in SEQ ID NO: 4, a thymine at position 14486 in SEQ ID NO: 4, a thymine at position 19910 in SEQ ID NO: 4, an adenine at position 20575 in SEQ ID NO: 4, a guanine at position 23716 in SEQ ID NO: 4, a guanine at position 23890 in SEQ ID NO: 4, an adenine at position 24995 in SEQ ID NO: 4, a cytosine at position 29099 in SEQ ID NO: 4, a thymine at position 33994 in SEQ ID NO: 4, a thymine at position 34942 in SEQ ID NO: 4, a thymine at position 37139 in SEQ ID NO: 4, a thymine at position 40233 in SEQ ID NO: 4, an adenine at position 40472 in SEQ ID NO: 4, a guanine at position 42831 in SEQ ID NO: 4, a guanine at position 42976 in SEQ ID NO: 4, a thymine at position 44195 in SEQ ID NO: 4, a thymine at position 48843 in SEQ ID NO: 4, an adenine at position 58556 in SEQ ID NO: 4, a guanine at position 59286 in SEQ ID NO: 4, an adenine at position 60217 in SEQ ID NO: 4, a cytosine at position 62826 in SEQ ID NO: 4, a thymine at position 62857 in SEQ ID NO: 4, a thymine at position 63400 in SEQ ID NO: 4, an adenine at position 63960 in SEQ ID NO: 4 and a cytosine at position 74909 in SEQ ID NO: 4.

25. An oligonucleotide comprising a nucleotide sequence complementary to a portion of the nucleotide sequence of (a), (b), (c), or (d) in claim 24, wherein the 3' end of the oligonucleotide is adjacent to a polymorphic variation associated with breast cancer.

26. A microarray comprising an isolated nucleic acid of claim 24 linked to a solid support.

27. An isolated polypeptide encoded by the isolated nucleic acid sequence of claim 24.

28. A method for identifying a candidate molecule that modulates cell proliferation, which comprises:

- (a) introducing a test molecule to a system which comprises a nucleic acid comprising a nucleotide sequence selected from the group consisting of:
 - (i) a nucleotide sequence in SEQ ID NO: 1-4;
 - (ii) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-4;
 - (iii) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-4;
 - (iv) a fragment of a nucleotide sequence of (i), (ii), or (iii); orintroducing a test molecule to a system which comprises a protein encoded by a nucleotide sequence of (i), (ii), (iii), or (iv); and
- (b) determining the presence or absence of an interaction between the test molecule and the nucleic acid or protein,

whereby the presence of an interaction between the test molecule and the nucleic acid or protein identifies the test molecule as a candidate molecule that modulates cell proliferation.

29. The method of claim 28, wherein the system is an animal.

30. The method of claim 28, wherein the system is a cell.

31. The method of claim 28, wherein the nucleotide sequence comprises one or more polymorphic variations associated with breast cancer.

32. The method of claim 28, wherein the one or more polymorphic variations associated with breast cancer are at one or more positions in claim 3, 6, 9 or 12.

33. A method for treating breast cancer in a subject, which comprises administering a candidate molecule identified by the method of claim 28 to a subject in need thereof, whereby the candidate molecule treats breast cancer in the subject.

34. A method for identifying a candidate therapeutic for treating breast cancer, which comprises:

- (a) introducing a test molecule to a system which comprises a nucleic acid comprising a nucleotide sequence selected from the group consisting of:
 - (i) a nucleotide sequence in SEQ ID NO: 1-4;

(ii) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-4;

(iii) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-4;

(iv) a fragment of a nucleotide sequence of (i), (ii), or (iii); or
introducing a test molecule to a system which comprises a protein encoded by a nucleotide sequence of (i), (ii), (iii), or (iv); and

(b) determining the presence or absence of an interaction between the test molecule and the nucleic acid or protein,

whereby the presence of an interaction between the test molecule and the nucleic acid or protein identifies the test molecule as a candidate therapeutic for treating breast cancer.

35. The method of claim 34, wherein the test molecule inhibits cell proliferation or cell metastasis.

36. A method for treating breast cancer in a subject, which comprises contacting one or more cells of a subject in need thereof with a nucleic acid, wherein the nucleic acid comprises a nucleotide sequence selected from the group consisting of:

- (a) a nucleotide sequence in SEQ ID NO: 1-4;
- (b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-4;
- (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-4;
- (d) a fragment of a nucleotide sequence of (a), (b), or (c); and
- (e) a nucleotide sequence complementary to the nucleotide sequences of (a), (b), (c), or (d);

whereby contacting the one or more cells of the subject with the nucleic acid treats breast cancer in the subject.

37. The method of claim 36, wherein the nucleic acid is RNA or PNA.

38. The method of claim 37, wherein the nucleic acid is duplex RNA.

39. A method for treating breast cancer in a subject, which comprises:
detecting the presence or absence of one or more polymorphic variations associated with breast cancer in a nucleic acid sample from a subject, wherein the one or more polymorphic variation are detected in a nucleotide sequence selected from the group consisting of:

- (a) a nucleotide sequence in SEQ ID NO: 1-4;
 - (b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-4;
 - (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-4;
 - (d) a fragment of a nucleotide sequence of (a), (b), or (c) comprising the polymorphic variation; and
- administering a breast cancer treatment to a subject in need thereof based upon the presence or absence of the one or more polymorphic variations in the nucleic acid sample.

40. The method of claim 39, wherein the one or more polymorphic variations are detected at one or more positions in claim 3, 6, 9 or 12.

41. The method of claim 39, wherein the breast cancer treatment comprises a nucleic acid comprising a nucleotide sequence complementary to a nucleotide sequence in SEQ ID NO: 1-4.

42. The method of claim 41, wherein the nucleic acid is a double stranded RNA.

43. The method of claim 39, which further comprises extracting and analyzing a tissue biopsy sample from the subject.

44. The method of claim 43, wherein the treatment is chemotherapy, surgery, radiation therapy, and combinations of the foregoing.

45. The method of claim 44, wherein the chemotherapy is selected from the group consisting of cyclophosphamide (Cytosan), methotrexate (Amethopterin, Mexate, Folex), fluorouracil (Fluorouracil, 5-Fu, Adrucil), cyclophosphamide, doxorubicin (Adriamycin), and combinations of the foregoing.

46. The method of claim 45, wherein the combinations are selected from the group consisting of cyclophosphamide (Cytosan), methotrexate (Amethopterin, Mexate, Folex), and fluorouracil (Fluorouracil, 5-Fu, Adrucil); cyclophosphamide, doxorubicin (Adriamycin), and fluorouracil; and doxorubicin and cyclophosphamide.

47. The method of claim 39, wherein the breast cancer treatment reduces breast cancer metastasis.

48. A method for detecting or preventing breast cancer in a subject, which comprises:
detecting the presence or absence of one or more polymorphic variations associated with breast cancer in a nucleic acid sample from a subject, wherein the polymorphic variation is detected in a nucleotide sequence selected from the group consisting of:

- (a) a nucleotide sequence in SEQ ID NO: 1-4;
- (b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-4;
- (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-4;
- (d) a fragment of a nucleotide sequence of (a), (b), or (c) comprising the polymorphic variation; and

administering a breast cancer prevention procedure or detection procedure to a subject in need thereof based upon the presence or absence of the one or more polymorphic variations in the nucleic acid sample.

49. The method of claim 48, wherein the one or more polymorphic variations are detected at one or more positions in wherein the one or more polymorphic variations are detected at one or more positions in claim 3, 6, 9 or 12.

50. The method of claim 48, wherein the breast cancer detection procedure is selected from the group consisting of a mammography, an early mammography program, a frequent mammography program, a biopsy procedure, a breast biopsy and biopsy from another tissue, a breast ultrasound and optionally ultrasound analysis of another tissue, breast magnetic resonance imaging (MRI) and optionally MRI analysis of another tissue, electrical impedance (T-scan) analysis of breast and optionally of another tissue, ductal lavage, nuclear medicine analysis (e.g., scintimammography), *BRCA1* and/or *BRCA2* sequence analysis results, thermal imaging of the breast and optionally of another tissue, and a combination of the foregoing.

51. The method of claim 48, wherein the breast cancer prevention procedure is selected from the group consisting of one or more selective hormone receptor modulators, one or more compositions that prevent production of hormones, one or more hormonal treatments, one or more biologic response modifiers, surgery, and drugs that delay or halt metastasis.

52. The method of claim 51, wherein the selective hormone receptor modulator is selected from the group consisting of tamoxifen, reloxifene, and toremifene; the composition that prevents production of hormones is an aromatase inhibitor selected from the group consisting of exemestane, letrozole, anastrozol, goserelin, and megestrol; the hormonal treatment is selected from

the group consisting of goserelin acetate and fulvestrant; the biologic response modifier is an antibody that specifically binds herceptin/HER2; the surgery is selected from the group consisting of lumpectomy and mastectomy; and the drug that delays or halts metastasis is pamidronate disodium.

53. A method of targeting information for preventing or treating breast cancer to a subject in need thereof, which comprises:

detecting the presence or absence of one or more polymorphic variations associated with breast cancer in a nucleic acid sample from a subject, wherein the polymorphic variation is detected in a nucleotide sequence selected from the group consisting of:

- (a) a nucleotide sequence in SEQ ID NO: 1-4;
- (b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-4;
- (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-4;
- (d) a fragment of a nucleotide sequence of (a), (b), or (c) comprising the polymorphic variation; and

directing information for preventing or treating breast cancer to a subject in need thereof based upon the presence or absence of the one or more polymorphic variations in the nucleic acid sample.

54. The method of claim 53, wherein the one or more polymorphic variations are detected at one or more positions in wherein the one or more polymorphic variations are detected at one or more positions in claim 3, 6, 9 or 12.

55. The method of claim 53, wherein the information comprises a description of a breast cancer detection procedure, a chemotherapeutic treatment, a surgical treatment, a radiation treatment, a preventative treatment of breast cancer, and combinations of the foregoing.

56. A method of selecting a subject that will respond to a treatment of breast cancer, which comprises:

detecting the presence or absence of one or more polymorphic variations associated with breast cancer in a nucleic acid sample from a subject, wherein the polymorphic variation is detected in a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO: 1-4;
- (b) a nucleotide sequence which encodes a polypeptide consisting of an amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-4 ;

(c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to an amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-4 ; and

(d) a fragment of a nucleotide sequence of (a), (b), or (c) comprising the polymorphic variation; and

selecting a subject that will respond to the breast cancer treatment based upon the presence or absence of the one or more polymorphic variations in the nucleic acid sample.

57. The method of claim 56, wherein the one or more polymorphic variations are at one or more positions in wherein the one or more polymorphic variations are detected at one or more positions in claim 3, 6, 9 or 12.

58. A composition comprising a breast cancer cell and an antibody that specifically binds to a protein, polypeptide or peptide encoded by a nucleotide sequence identical to or 90% or more identical to a nucleotide sequence in SEQ ID NO: 1-8.

59. The composition of claim 58, wherein the antibody specifically binds to an epitope that comprises a glutamine at amino acid position 278 in SEQ ID NO: 9 or a glycine at amino acid position 389 in SEQ ID NO: 12.

60. A composition comprising a breast cancer cell and a RNA, DNA, PNA or ribozyme molecule comprising a nucleotide sequence identical to or 90% or more identical to a portion of a nucleotide sequence in SEQ ID NO: 1-8.

61. The composition of claim 60, wherein the RNA molecule is a short inhibitory RNA molecule.

FIGURE 1-A

>3:198232901-198309500

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1      actaagttac tacaaagcag ttaacatagt ctcagatatt aaaaatttaa gatactgaag
61     agctaagtca attcctgata atttctttaa tttgtgatct atttctttca ctgtattcag
121    atcttcatat ttRtagtctt tgcttagagt cttcccaccc gcccccacct cgctctgttg
181    ctcaggccgg agtgccagtg tgcaattccg gctcatcgca gcttctgcct cctgggttca
241    agtgattctt gtgcctcagc ctccctcagta gctgaaatta caggatgtga ccaccatgcc
301    tgtttaattt ttagttagt agagacagag tttcatcaag ttggccaggc tggctctgaa
361    ctccctgctt caagggattt gcctgctttg gcctcccaaa gtgctgggat tacaggcgtg
421    agccattgcy cctggccaag tctttgcctt actcttaaca attcctcaca gctaccttcc
481    tatatgttca aaacataactt cggcattttt aagttaactt tcctttaaac cttctatttc
541    atttacctac ttaagattcc taccttttcc ttttgtttca atcaattgat acttttagtc
601    ctatcagttt ccacatttta cctatccctgt gtatattttc gtaataactc ccaccaacat
661    atttttgttt tgtttttaag gtttttttgg agacaggctc ttgctctgtc atccaggctg
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781    cctaccttag cctctcaagt agctgagcct acaggcatgc atcactatgc ccagctcatt
841    tttaaaatta cttgcagcga cagggtgtcc tatgttacc aggggatctt caactcttag
901    gctcaagtga tctcttgtc tcagcctccc gaagtgtcaa ccactacacc tattttctta
961    aatttttatt ttgacggaag agtttcatcc cttttttcag ttaagtcaat tacactctc
1021   tcctagaatt acatcaaaac tcagcaaagc tataatttta cataagagat tttctccatt
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1141   atctgaactg ctggctacaa gttagtatgt atacgcttat acaaggagag atatttaaaa
1201   gctgattttt tcatttgata tcccctttca aattttaacc tttgttttca cgcgcacact
1261   agaagtaaaa agtgagggaag gggtagggg gaaattggac ttcctcaatc tcttctaac
1321   atgcaatccc tataaagaaa aacattcatt tataactgta ataaaataca ttaaacacag
1381   atattaaacc caagagaaac aattctcaga gtagggatac tattaattgg cctaaagaaa
1441   aagggaaact atttttaaga aggccagtta gttgttttaa gtacaatagc tctctggcat
1501   actcggagga ttagttccag aaccccacgt ataccaaaac ccgtgcatgt tcaagtctaa
1561   caggaggcct tgtggaatct gacaggcata tggcattttc tatcccagtt tggttgaaca
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1681   acaggcgctg agaaaaatac agcaagggaa gtgggaaagc aggagactga aaaaaatttt
1741   aattacctat ctactactga aaatgataag aaatgacaaa tgtctgcaaa taaatgccac
1801   tagtccactg caatcttccc agattatctc cactcttctt ccctttgggt ggtataagaa
1861   gtaataatga aaataaagtc aggacactgg gtgttagaaa tctacctttg taactcaaga
1921   tttcaatcaa agctttgaag cgcagaaaag ttaagtgact atggcctaac ctctctagac
1981   tctgggtcact tgcaaaatag ggattatgcc accaaacagt tttttcttgc cgaaaataaa
2041   atatgtcaca aatataagac ctaaccaatg ggaagagaaa aataaattta acttatatat
2101   tgagtttctt tccaatttat ttcttttatg gtattattac aatataatta atgctttctg
2161   aacaaaagat tgagatataa gctctgaaag ttggcctaata actcttgagg aacaataaga
2221   ttaaatattt gaggtgagag attccaagag tttaatgagt agttgaaaga gtaagaacag
2281   ggtatggaga cccaccacga accccagagt tggcacaagc attttaagct gaagatatct
2341   gagattcaac agatgcagga aaaaagcctt ctccggagtt ctctaactct actaaaaggt
2401   gcagcttccg agaaatgaag ttaccataaa taccctctga ggagtcgatg ggcccgagag
2461   aatggaaaga ccagtcatac cagtttagac aaatgtcatc acaaacttta tccccatct
2521   cttctcctaa aaacttgtct ttccctgaaga aatgtacgtt tttctaataa aagctgtttc
2581   tccctccttc ctttccctac tagattaggt gtacaagctt ttaacttcat ccacaagcta
2641   gcttcagtat ttcttctgtt gcctcttgca tccatataca agaaactttt tttccatggt
2701   aatctgtttt ttttctcagt ttacttcaca ggcctgttac tgaacataca aggtggagg
2761   aaaaggtttt tcttcgctta aaaggggcta gaagaaatct taaccgttta acagtttgtg
2821   aactagcaaa ttacttggtc tctttatgga agagcttatt caactacaac gtaaaacggg
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2941   gggtcgtatc atgcatggcg tacagtttta ctattatata ctatcacagg agattctttt
3001   ttttttttgg agacagagtc tcgctctgtc gccaggctg gactgcagtg gcgtgatctc
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3121   agctgggact acaggtgccc gccaccacgc ctggctaatt ttggttttgt attttagta
3181   gagacggggt ttcaccgtgt tagccagaat ggtctctatc tcctgacctc gtgatctgcc
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3601   aatcctccca ctaggcctt ccaaagtgct gggattagag gcctgagcca ccagtcacag
3661   ctaattttctg ataattgattc tccaaaaaga ttaacagtaa agggccccc aagtgaatta

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FIGURE 1-B

3721	ttccttgcct	ttggaattaa	taaaactgaa	aggagttaga	agataatggt	ccttcatatg
3781	tcttgttagag	attatittttt	ctcataatca	gaatccaagt	caagaaagtt	caaagtacac
3841	aagctgaaaa	acccataaaa	gtactttttt	ggaagactaa	taaggcaaac	catagatcct
3901	gaaagataaa	aaacttaatt	ctacccaaaag	cttacctttg	tctctatctg	tctgtcttgt
3961	atgtatatat	ataagattat	caacaaggca	gagaatccca	agccttttagg	aaagatacta
4021	actgcaagat	gctgattatc	agagtgtcgg	atgactcctt	ttgtactttct	taaaatccga
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4261	cagatcacct	gaggtcagga	gaccagtctg	gccaacatgg	tgaaccccg	tcgctattaa
4321	aaatacaaaa	ataagccggg	cgtgggtgga	ggtgcctgta	atcccaccta	cttggggaggc
4381	ttgaacctgg	gaggcgagg	ttacagttag	ccgagattgt	gccactgcac	tccagcctgg
4441	gcaagagagt	gaaactccat	cttaaaacaa	acaaaaaaa	ttacttatta	ctttgctaga
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6241	tcgcaccact	gcactccagc	ctgggcagta	agagtggaa	cccgctctca	caaacaaaaa
6301	acaaaaacca	aaaaaaacca	aaaaaacaaa	caacttttga	tctggaaaaa	gaactaggtt
6361	cagactaaac	aaatactgga	ttagcaaatc	agaaaaaaag	cacaaaaaaag	gaagtttagc
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6841	aacaaaaaca	ttttcccta	gaaggctggg	tatcaatcca	ttgagaaatg	taccttaatt
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6961	caatgggagg	gaaagtcatt	ttgctttag	catccattta	cctcctgcc	cattctcacg
7021	cctactgtct	aattcagttc	caattatttt	tcttctgtga	caaactaaaa	cttccattct
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7141	gatttaatta	gaataaatgt	taattaaatg	aaccaggagt	tattttttga	attaagagcc
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7261	gaggcaactt	aattcttatt	tctcaaaggt	taccaatact	ttgcgcgcat	atatacatat
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7441	aattaagaag	caacaatgaa	tagaatatgg	caatgttcag	gaccttcact	gaaaattttt
7501	ggaaaggaac	gatcatcatg	caattttttac	acaaaaactt	gttttgttga	gaactaatct

FIGURE 1-C

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7561.   aaaatctggt aaagatcaca tatcactttt aaaaaatttg actatgagcc cagaaattct
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7681.   atctaaaaag aaaccattat gcaactaaat ttaaatacat accccttgag gctgggcatg
7741.   gtggctcaca cctgttatcc cagcactttg ggaagctgag gtgggtggtt cacttgaggc
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8881.   tggctcacgc ctgtaatccc agcactttgg gaggccaag gaggcagatc cagggtcag
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10081. tttaaatcta tggaaattct ctatttcttc ttgagttagt ttcagtatt tatgtctttc
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10621. tatatttgtt agtcaattttc ttagtggtta tcttggatta taagtaaaaa tttaaagcca
10681. gatgtgggtg ttctagactg taatcccagt gactcagggtg gctcaggcaa aaggactgaa
10741. gcaggagcat cacttgagta caacactttg agggctggct aggcacaca gtgagaccct
10801. tatctctaaa aaaataaaga aaacaattca gccagggtga gtggtgcata cctgcagccc
10861. agctactcgg gaggtgagg cacgaggagt gcctgagtaa gtttgaggct gcagtgaact
10921. atgactgtgc tactgcactc cagcctgggg gacagagtga gatgctgcct ctaaaaaata
10981. ataagtaaac aaacaaacat tttataagaa cctagtttct ttaccgcct tgtggtgttg
11041. tcatattaat tttatgttta tacgatgtgt gcacatcaa tttgtaatta ttgctttatt
11101. cagttgtttt taaaatcagg ttggagaaaa aaagagttgc atataaaaca atacccttat
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11281. ggcaggtttt tgagagatga actccttcag cttttgttta tctggcaatg tctgtatttc
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FIGURE 1-D

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11401 cttttcagaa ttttgaatit gttatttcac tgctttctga cctccatggt ttctgatgag
11461 aaatcagcta ttaaccttgt tgaggatccc ttgcacgtgg tgagtcattt ctttttgcta
11521 ctttcaatat tctgccttcg gcttttagaca gttcgattgt aatgtgtcta tgtttagat
11581 ctctttaaat taatttaact tggagttcac tgaggttctt ggattaatgg ttttaataca
11641 gttctagaag tttttgggag agtattttatt caaatattct ttcttctttt ttctctcttt
11701 cccatctttc acatactccc attatgttgg taaatttgat agtatcccat aggtctctga
11761 agctgttaat ttttcttcat tctttctttc tttgttattg ttccagttctt cagcatcaaa
11821 atctcaattg acccatcttc aagttttgctg attctttctt ctgccagctc aaatctgctg
11881 ttgaccttgt ctagagaatt tttcatttaa gttactgtac ttccaactc cagaatttct
11941 atttggttct tacatataat ttctaactct ttattgatat tttttacatg gtgagatatt
12001 gttcctttac tttcatgtca gtctacagga tgggttttctt ttattccttg aacgtattta
12061 aaatacctgg tttaatgtct ttgttttagca tgttcaatgt ctgaccttcc cttaggaacga
12121 tatccattga ttgcgttttt ctcctgtata tgggccatac ttttctttcc gcttgtctca
12181 aaattttatg acgaaaaata ggcattttaa ataaatataa tacggcaact ccagatagca
12241 gaactgtcct cttatctacg cttgtcattg ctgtctgtta gtgacttttc ttaatgttat
12301 aaagtccgta ttctttgttg tgtgtggcca ctgaggtctc tgtctgggta gcttagtggt
12361 taatgactga atacatattt ccttaaatca ctgaaactta caaatcttcc actcttttcc
12421 aagggttata tgtgcatttt ggggcccaac ttttaacact agataagcaa ttaacaactg
12481 ccttaaatcg cttgcacaga ggtcatgat caggtagagg tgagagttta aggccttttc
12541 tagtctttcc tgagcatgag cacagccctg aacatgtgtg tggccttctg gttccaagga
12601 tacacggagg ttttcaaagg ccttatggag aattcactcc tccaattttc cttttaagtt
12661 tattgatcgg tctactattt cctagtgttt ttagggcatt tccctagaga agttcagtaa
12721 gcattaaaaa ttttaaggta ctgatgcata ttgctaaaca taatgtctga ttttaactga
12781 ctacacattag ggtgagctac ttccctggac tagctgagac ttccagtttt agaataagaa
12841 ccaaagggtt tccagacatg gggcattcag ttctaaaacc atgaatgttc tgggtgaact
12901 aggttgagtt ggttgggtct acacacttta gcactgtatc aatgacctat ctaaagtggt
12961 tccaaaggga caatttaaaa acatctatta ctgaactcta ggctaaacga aaatttatit
13021 ggacacaagg tgtgaagtga ggtcttaagc taattttatt tccctaaata actaggtaat
13081 atgttcaaca atattaatct ttttaagcca ttccctacca ctaagttttc cttatcatac
13141 tgtaacttaa ataaattaca gtatatttta caatgaaatg tagaaatttg aacagctcag
13201 ctgaaaggat tttgctaacc Rtaaaaatca tgaaaccact accccagaca agacatgtat
13261 cttttccacc gatgttcaac tgtgcacttc tatagtcatg cccaatcact ggcaaccact
13321 ttctgactta cagcaccaca agttagtgtc acctgtctct gattatcatg taactggaat
13381 tatatagatt gtatttttgt tatctgtttt gctcaacata cttgttttgt gtttcagtag
13441 ttgttccttt taattgctga gtagtattat attgtgtaaa cataccacaa tttagcaatt
13501 gtcctgctga tggaaacctg ggtcatttca aggtctagat tattatgaat aaggttggtta
13561 agaattgttct tgtcaaagtg tttttgttga tgtatgcttt catttgcctt gggtaaaacc
13621 tgggtgataa gattagatgt atgttttaact tcttaaaaac cttcccaaaa gttctttag
13681 tgggtatacca tttacacgtc cactagtagt gaatgagggt tgtagctgct ccacatcctc
13741 atcaatgaat gttgttattt ttttcttttg ttgttcaact aagtgggata tagtatttca
13801 ttacgacttc aagaatacct atttttatct aggcataatc aatcttcttt agtgatatgt
13861 taagttttgg caaatgtgaa tttcgtgcag ccaccacaa tcaaaaataa gaacaattac
13921 atcactctta ttcaactccc tacaaacctc ttcattcact gcggtttgtg caactctctg
13981 atgcctaatt ttaagcacct tttcatgtgc ttactggcca ttcacatata ttttgtgctg
14041 tacctgctca agtcttttgt gcatttttaa ttgggttatt catcttttta ttgttgattt
14101 gtaggagata tttatatatt gtggatacaa gtagtatgtc atgtatgtgc tgagaatatt
14161 ttttaccact gtgtggcttg cctattttgt ttttttctt cttttttttt gagacagggt
14221 gttgctctgt tgcccaggct ggagtgcagt ggtgggatca aagctcactc actgtagctt
14281 caaacacctc agctcaagtg atcctcctgc cttagcctcc caagttgctg ggactacaag
14341 tgcccactac tatgtctggc taattaaaaa aaaatttttt ttttaaagat ggggtcttgc
14401 tatattgatc aggttggtct caaacgcctg gcctcaggcg atccacctgc ctcagctcc
14461 tgagttactg ggattataag caagatgcac gtcacccagc gtatttggtt tcttaatgtc
14521 atcttcttta tgggttagtgt tttatgcatt ttgtccaagg aactgttacc tacttaggc
14581 ctgtgaacat agtctctgat attttcttct aggaagatta tggttctgag ttttatattt
14641 agatctataa tccatctaga attaaatttt atgtctggag taagactggg ttaggtttat
14701 aattttatat acagatatct aggtattata gcaccatttg ttaaaaagat tttcccttct
14761 ctattgaaat gacttggtgg cctcttggtta ctatttaaga aatttgtcta atccatattt
14821 actaagattt tcttgatgt tttcttttag aagtttagtt ctatggtoca tttcaagtta
14881 atttttctat acaacatgaa gtaagaaatg agattcttct tcttttctt gtgtctactt
14941 gttctatcaa ttaaagaaga gggcatttaa atctocaaat gtgactgtag atttgtccat
15001 ttccttccct agttctgata atttatactt catgtatttt gaaagtatta ctaggtatgt
15061 cttcttgatg aaatgacact tttatcttct tctgtcttct tataattatg aaatctatgt
15121 ataataacat tatttctctt aaattctatt ttgtctcata ttaagacagt agcttttagta
15181 tgctatttgc atagtgtacc ttttttctct tttacttaca acccatgaac ctttatattt

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FIGURE 1-E

15241	aaagtaaatt	tctgataaac	agtatatagt	ttgggtcttgc	ttttttgaac	caagccgaca
15301	atttctgtat	cttaaaatcg	tagcttttaa	gattagataa	agaaaattta	agctgctata
15361	gtttcagatt	agatatagat	aagatatagt	taagatacag	ttataggtaa	ggtatagata
15421	agatgtagtt	tcagattaga	tatagataag	aaaattgaag	ctgctacagt	ttcagcttct
15481	tgggaggctc	aggcaggaat	atcgtttgag	cccgttaagt	tgaggctata	atagtgtctc
15541	atgattgtgc	ctgtgaatag	ccactgtact	ccagcctagg	caatgcactg	aagccctgtc
15601	tcttaaaaaa	taaaagaaa	aaaaaagaaa	agaaaattta	taaacttgaa	ttacaaggag
15661	acagagctgt	aaatatgaaa	ttgggggttaa	cagacatgaa	aaacagattc	acatccactc
15721	ataggagttt	agggacagag	tacatacaac	atgggaaaag	caaaatttga	aaagacaatg
15781	gctaagtctt	cagaattgat	gagagaagtt	tttagaattg	atgaaagaca	tgactcctct
15841	gactcagtag	gcataatgaa	tcccaaaccac	aataaataat	atgctagaca	tcgacaaagt
15901	ttcacatttt	agtgaactcg	cagcacatca	aacacaaaag	atcttacaag	cagccagcaa
15961	acccccacaa	gtcacctacg	aacaagacag	agtagacttc	tttcgttaaa	tagaaaacaac
16021	acgccagaca	acataaaaaca	gtatcttcaa	aatactgaga	ggtaaacagct	atcaactctg
16081	gtaattctag	attgaactaa	cttttaaaagt	gaaataaaat	aaagatactt	tcagataaag
16141	tctagaatat	ttacgattaa	ggaaccattg	ctgaaagcac	aatcaaggg	cttgacactc
16201	aagggtgcatt	tagatatctg	aagggcattt	ttgcttttta	caatgactag	ggagttttac
16261	tagcatgtag	catgtatatg	aaagctttta	aaaaagggaa	attttcggcc	aggtgcagtg
16321	gtcacgcctc	gtagtcocgg	cactttggga	ggccgaggtg	ggaggatcac	gaggtcagg
16381	gatcgagacc	atcctgggta	acaaggtgaa	accccgctctc	taaaaataca	aaaaaattag
16441	ccaggcggtg	tggcgggtgc	ctgtagtccc	agctactagg	gaagctgagg	caggagaatg
16501	gcatgaaccc	gggaggcgga	gcttgcagtg	agccaagatc	gcgccactgc	actccatcca
16561	gcttgggcaa	cagagcgaga	ctccatctca	aggaaaaaaa	aaaaaaaaaa	aaaaaaggga
16621	aattttctat	gaagagcaag	acagtcctat	acaacaaata	actgtacaat	ccaaatgctg
16681	ttagtgggtc	actgagaaac	acagaagagg	gaagatacaa	gatgggacgg	taaacaaaaa
16741	ttgtatgacc	tgtggattaa	cttttaataa	acaaaaataa	aaattacaat	ttatgggtat
16801	aaacatgaaa	cagaagtaaa	atactagaaa	tggcatgatt	agaattaaag	tttcccaaa
16861	tctgtgtgtc	acagtagaac	tataggttaag	ttttagacaa	aaattgtgta	tgggtaacaa
16921	cataagcaca	caaattgaaa	gtaagaaag	gagaaaaag	gacacaaata	tcaagccaaa
16981	aaaaaaaaat	cagccacatt	aatagcagac	aatatagatt	ctagggttaa	accactatta
17041	taaatcaaga	tgttcattac	ataataacaa	ctataaaaact	atgtgtaccc	aataatacaa
17101	tttcaaaaga	catactaaaa	aaacctaata	ctatgaggac	caactgttga	acccatgttt
17161	gggtagcttt	aaaaaaatca	tatttgcata	gctttcaaaa	cctcaataga	tcaagaaggt
17221	aacagattaa	agtataaaga	agtacacaa	taacaaaact	gagttaatag	acacatagca
17281	aactttctYag	tcaataaata	gagaacacat	aatttcttca	agcacattta	taaaaactga
17341	cccctttcta	taaaagaaca	cctattatat	aatatgttct	ctgacactac	aattctacaa
17401	ttaagctgta	aaatgttaag	aagataacca	agatatcccc	attacttttag	gatataaaaa
17461	aacagaagac	cttgccttaa	aaataggctc	agtgaataa	acaaaaacgt	gatcttgact
17521	aacgtgtctt	accgatataa	tacgatctcc	ttttctgagc	tctccactta	gatcagcagg
17581	tcctccggct	aagataaagg	aaataaatat	tccttctcca	tcttctcctc	ctacaatgtt
17641	gaaaccaagg	cccgttgagc	cacgatgaag	aacaactttt	ctagggtccc	taaaaattaa
17701	aaaaaattga	gtatcttgga	aattttatat	aaaacctgac	attctatcag	tgagaactac
17761	ctactgataa	tttttatgtt	atcaaaactac	aaagaaaagct	agacaaaata	taaatggttt
17821	ttctaaaact	acgagataaa	gagattctaa	gcctacaaat	caaaggaaaa	aatctaattt
17881	tatataaaag	caaaaaacct	gtgttatata	aaacagaaat	gaaaccaaaa	cagaaaaaaa
17941	acgtggaaat	ttaaaagtat	tataagagct	tatcaggaaa	tacacatact	catgaaaagc
18001	tgatgttgca	cactttattg	ccttcaaagg	aatcactgcc	cctacttaga	agtttaaaag
18061	gcaggatctc	ttttgtctta	gagaaggcag	gccctttctc	cagtctcaaa	gggatgaacc
18121	ataaccaacc	taaacaagtt	attgcaatcc	catgcccott	tgctgaggtg	agagtataac
18181	ccatttctaa	cctctggtaa	atgaagggaa	attttattgt	cattttctag	agacagacaa
18241	accttatcaa	ggacaaagca	tctttgctac	cttcctttcc	tcaaaaaaac	gaaacaaaat
18301	aaacaaaacc	ccacacgact	gaataatata	atccctttac	tggtttggac	atattataat
18361	caggaaggtg	aaaccaagag	tataccgaag	acaccacagg	cctaaggttg	ctataccaac
18421	cttggaatag	cccatcttca	ggctttttat	atgaaataat	taaaacctat	ctgcaggggc
18481	acaggtaggt	tttatcatat	tagtgatgtt	ttatttctta	aattagatgg	tgaattccgg
18541	atttactgtt	cccatatgac	tttaaaatat	gtatgaatta	gaattttata	ttaggaaatt
18601	atacttgatt	aaaaaatact	cagctgaaat	tcaacagtat	ttccagggga	aaatacactc
18661	tgattttcaa	ataatgtaag	cacatgaaaa	ggtgctcaac	atcatcagtc	actagggaaa
18721	gagatataaa	aataatgaga	tacttcaggt	ctactaggat	ggctatttaa	aaaaccacaa
18781	aacaaaaagt	aacaagtgtt	gatgaggatg	taaagaaatt	gcaactcaca	cattactgat
18841	gagaatataa	aacggtgcag	gcactacgaa	aaccagtttg	gtggttcttc	agaaagctaa
18901	catagaatta	ccatagtact	cagcaattcc	acccttaggt	atatatccca	agtaactgaa
18961	agcagtgtat	tgacagata	cttgatgcc	agtgtttatt	atagaattac	tcacaataac
19021	caaaagggtga	aaataactca	agtgcccatc	attagatgaa	taaacaaaat	gtggcatata

FIGURE 1-F

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19081  tgtataattg aacagtattg tcataaaaaac aaatgaaatt ctgatacatg ctaacaaatg
19141  agtgtatctt gacaacataa gtgaaatagg ccagtcacaa aaggacaaat attatacagt
19201  tccactttta taaactatcc agaataggca aattcataga gacaaaaagt agattaaagg
19261  ttaccagggg ctgggaagac agtggaaggg agaattactg cttaatggtc acagagtttg
19321  tctgaagtaa tgaaaagggt ttggaaatag tgaagggttc cgaaaattgt gaatgcaatt
19381  aacactactg aattgtacac ttaaaaatag ttaaaatgtc aaattttggt atatatattt
19441  cgctacaatt tttaaaaact gatgtaatat accacaaatt gtatacttta aacagggtgaa
19501  atttatgata tgtgaatcat atctcaataa agctgttaaa aaataaactt tagaaccaa
19561  atgtaggtat gttgtgattt ttttttttac ttttttgata ttggtaacat ctgaaagact
19621  gcttaaaagt aaattgtgaa gaacttataa tgttggaag attttatact tcattattac
19681  aaagtagtgt gattatcaaa agggagtggg tcatacttaa aagtccaatg caatattcta
19741  gacaagagac tcaagtgaag aagcatgagg aacagtaatc aagggtgcaa tataacttat
19801  tttttagttt gtaaaatatg caaagagatt aaagactaga taagccattc actattacag
19861  tttccctctt tacggcctta aataggcact attagaaagt aataaaaaata aatggcaatg
19921  aaaggctcact ctagaagcac tgcctgaaga ctagcagcct tggatattcc catcacaac
19981  aaataagaac actattcttt ctgctaattt tcatcccaa cacaattact gacaacctat
20041  taagtttcca acattgctaa ttctttatga aagaaaagag acaaactctc ctatctgtcc
20101  taaagatcac tgcctagaat caggagtctg ataagtaaaa aataataata atgctaacaa
20161  taatgtaatc aataaacgtt aagaacagac attacttagt acacatttta atgttgaatc
20221  tgtaataata aagacgtgta caaattacaa agcaaactct atagtgtctt attactatat
20281  tgaataatat gaaaaagatc tacaatgctt tttcaccaat tttttctac ctcattagaa
20341  ttctttggga ttaaaaagac agttaatcta tacatttcag tgcaggtagt aatttttagt
20401  gaaagtaaat tttgtgtgtc agaatatcaa ggatataatg caaacaacaa aatccacca
20461  ccagccaggc aaaggggatc acgcctgtaa tcttagtacc tagggaggca gatacgggag
20521  gatagcttga gtctaggagt tggaggctgc agtgatgtac gttcatagca ctgcactcca
20581  gcctgggcaa cagagtaaga ccctcctgct aaaaccaaac caaaccacca cttattgaat
20641  tctgaacaca aatcaaataa ctgccatatt tttatgggat atattagata aggaacatat
20701  aaaaatgtac tttaaaatat gcataagaat tttcttaact tagttttact aagctaattc
20761  ctaaggacaa tttaccaagc ctcaaagaaa agcagtatta attttaaaaa aggagtggta
20821  atttatttgt aaaaataaaa catgtatatt tcaggctctt caatgaatcc tcctatggaa
20881  aaaaattaac ctttaagctc actaactgtc aataaaattt tttagtcta aaaattgtgg
20941  ctatcttaca tggttgatta aaattcaatt taatagtgtg ttttatgtaa gaaggataaa
21001  tgttaacttc ctacacttgt aatttcatca tctccaagta ctgctttaga aactggggag
21061  tatctggctg gagatgctgg tgtctggccc aagaaggaag atgggctaac atggttatca
21121  acaggctgag aagaagcttc aaaataaaca aagtgaaaaa tacttcaaac acgaaacaag
21181  ccaatcagta ttccatttat gagtgtatga tgtgtaatat atatgcactc ctttatatat
21241  cagaatttgg tagagaagat ttactcatca gccaaaaaac tggacattat gttgccagg
21301  ttagtctcaa actcctgtcc tgaagtgata ctcccacctc agcctcccaa agtgttggga
21361  ttacaggcat aagccaccac accagatta cttaaagaat tatatacagt ccaaatttga
21421  ttgtgaataa taaaatcag aggttttcca ataagtgcga aaagactatg tccttatact
21481  agctcagatc tgtcaaccta atttacatct atgtctttta attcacccat agaagaataa
21541  aaacctggta aaaagcaaaa acgaaaaaca agcaaaaact gtcgtccagg cgtagtggct
21601  cacgcctgta accctagcac tttgggagcc caaggcaggc ggatcacctg aggtcaggag
21661  ttgcgacca gcctggccaa catgttgaaa tcccatctct accaaaaaaa taaaaaatt
21721  agecagactt ggtggtgtgg cctgtagtcc cacttactcg ggaggctgag gtgggagaat
21781  tgcttgaacc tgggaggtgg aggttgcagt gagccgagat cgcatcactg cactccagcc
21841  tacgtagggt acagagttag atgccctgtc tcgagaaaga aaaaaaaaaa aaaaaaagca
21901  aaaaccaaac gttggttcac ttcaatagta ataaatacca catataggtt ttccattcta
21961  gcaaaagcta ataacagaaa attatagtga ttctgacca tgctttctaa agacacaggt
22021  aggtaacaca tggcagctgt agcttcaaaa gacataagac acttgaatta ttccaatcat
22081  taccaaaaca cagaggaagc aatatttaac tttcttgagg cttcaactat gataaagtta
22141  caaagcactt caaaagtagc tgtattattt aattatcaag cattaatctc ttttttatta
22201  aattagagca tatcttctat ggagggaaag agcatactac gcactggagt acaaaaaatgc
22261  aggaattatt agttcaaat actatagtgg ccagataggt aacataaagg aataaagtga
22321  actggatgaa agacaacagg aaatgactga aacgatagta ttttagagat gcagtgtatc
22381  tattgatatt acaggtttgc agtatccaac agcaattgtt tcctatccag ttcatatata
22441  agatgctcgt ttgtatttga gccaaaggac tttctaccaa tggctcttaa ctttgaaagt
22501  ccaaagtctt tcctgggtgg tcagtaagaa tatgggattt tcaagtgaat tggatgtag
22561  cctcaatca atagataccc acgtgaacct ctacaatcac tagcctgtta aaaatccaga
22621  gtttactgat ttttgactct taaattcttt tgctgcattt tcatatttag atgaaacaaa
22681  aaaaacaact agacaagaaa tccagtcaaa tgcccaaacc agaaaatata cattttccct
22741  gacacatcca gactatccct ttagtcaatg catcctttct ggggcagtta atctcacatg
22801  taccacatac tctcagacaa cagagactaa aaattaatgt tcctatgaaa gaaatgacgg
22861  cctcaaagaa ggatcagata aaacagtact atttcttata ccccaatct tatgtaaaaa

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FIGURE 1-G

22921	gggtcccccag	agaagcacaa	gagtgcctaa	ttcatttttc	ttatatatta	agatgaatga
22981	ttcaacacta	taagatttta	tagaaaaagca	agtagaagag	cttgaagtga	gaatgggaaa
23041	agactgggtg	ccaaatcaga	agtagcaagg	ccatgcagct	aaagagaata	taagttaaaa
23101	gcgagaaaat	atatactgta	aaaaacagga	acattttaat	gtcggcagag	aaactgtatt
23161	ctctgtttaga	ttcaacagac	ttcttttttt	tcctactttt	attcctgagt	atcatatttt
23221	gactacctta	ttttggttat	aaacattgtg	gctctttatc	ttctatagtt	catgtataac
23281	ttctatgatc	ttccctattt	cttttactat	tcttgctaaa	aatatttttc	taactagtac
23341	aaaaattggt	ttccaatttt	gacatctgct	cacttgcaag	gctgcctctg	tgagaaacat
23401	cccctccatc	aatgcttgac	aatcaccaca	aaaaaaaaa	aaaaaaaaa	tcaaatgtta
23461	tctagtcctc	ttaggtaaca	agagaaagaa	aatctgaaca	ttcttgtgtc	tgctaaggaa
23521	aatgcattca	gaactaaaa	ccttcccaag	aaaactccag	ggccagacag	atagatagct
23581	tcattggaaa	attcaacaaa	acatctagag	atgaaataac	attctgaaac	attacaagac
23641	agaaaaattt	caggacacta	tcgttaagtt	catgcttggtg	aacacagatg	taaacctaaa
23701	caaaatataa	gcagttcaaa	atcaatgata	tataatata	attataagga	tgtgggtttt
23761	ttccccccac	aaatgaatgg	tttagcgtta	gaaaatcaat	gtaattttatc	acgttaacaa
23821	aataaaaagag	aaaaatcatc	tccataaata	attggataaa	attcaatact	tacaggataa
23881	aaactcccca	taaaccagga	ataaagatta	actttcttaa	tacaaaaagg	gtatctacag
23941	aagacctgct	ggtaacacca	tatacaattg	tgaaatactg	tgtccccag	tttgtgaaca
24001	tgacagtgat	atttattatc	accattttctg	ttcaacactg	aactggaggt	cttaccaatg
24061	catcagacaa	gaaaaaagaa	aatgaacagt	ataaagatag	gaaagaagga	agtaaaattc
24121	attgttcaca	gatgacatgg	ttatatacgt	agacgatctg	aaagacctat	aaaacctaac
24181	attacaagaat	ttagcaagat	tggttgactaa	gcaatttaata	tacaaaacag	atatttccta
24241	tatatcagtt	aaaattagaa	acattttcaa	agtagtacat	ttataatagc	atgaaaaaca
24301	tcaaatagcc	aggactaaat	ctaacatata	aaacctctac	tataacaacac	tgacagagaga
24361	atgtaagaag	gacttcaata	aaagaagaga	tattcatatt	aatggactga	ttaagaaact
24421	caatttaatt	cttcctaaac	cgatctgtaa	tgtttttgat	cctaaaatta	aaaaggaaat
24481	tcaaggaccc	aacataatct	tgaacagtaa	caaaattaa	atttacttta	catcaatatt
24541	tattataaaa	ttatgataat	taagagactg	cagggtggtac	aaagacaaat	agttcaatga
24601	aacagaagag	cctagaaaata	ggttcatata	tatgtggtca	cttaaaaagaa	aagcaccaat
24661	gcaattcagt	ggcagaaatg	gtctttcaat	aaatgatgct	agatcaatta	tatatctgca
24721	tattaaaaaa	tctctcatta	catgcaaaaa	ttagatcaaa	atggatcgga	cctaaatgtg
24781	aaaggcaaaa	tactaaagct	cctacaagtc	ccttatgacc	taaggatagg	aaaaatttca
24841	acaggctact	aaaagcacta	ccttaataga	aaagactgat	aaggaaattaa	aaaattttat
24901	ccatcaaaaa	gtaccattgt	tttgagggaa	aacataaaact	cagtgaagac	atctgcaaca
24961	gatgtaactg	attagagtta	tttctcaaat	acataaaact	tccttttaaat	caataataaa
25021	accaatggaa	aaatgtaaaa	agatttgaac	agacattgca	ttgaacaaga	gtcaaagcaa
25081	taagcacagg	caaaaatgct	gaaaataaatt	aatcatcagg	aacaaccagc	aataaatgaa
25141	taaataataa	tcattaaaa	catgagataa	ctttatacat	atacatacta	ttcataatta
25201	aaaagatgga	taataccaag	ggttggtgag	gatgtagaaa	aactggggtc	ttaattgcct
25261	cctatactgt	tgaaattggt	cagcagtatc	cgctggagac	taaacatatg	cctaccctgt
25321	aacacagcaa	cctcactcca	tgagaaatga	ctgcttatgt	ctgacaagga	tgtgcaaaaa
25381	catccacagc	agctacactc	ataaaagatc	agaactgtaa	gtgactcaac	agtaaaatga
25441	aaaaaattgt	tgtacactta	tacaatggaa	taatacatag	cagtttttaa	aagccatgtg
25501	actgatcatt	aagctaaatt	cttaaaattg	gtacccttac	tgaatatatg	ttttaattca
25561	attaaaaaatt	aaataaagag	gtcaggtgca	gtggctccta	tctgcaatcc	caacactttg
25621	ggggcactga	ggcaggatca	cttgaggtta	ggagcttagg	caacatagtg	agaccccatc
25681	tctacaaaac	aatttttaaa	attagctggg	catgctatcc	tagacacttg	gRaggctgat
25741	gtgggaggat	ggcctgagcc	caggaattca	aggctacaag	gaactatcat	cgtgtcactc
25801	cactgcagcc	tgagcagctg	agtgagatcc	tgtctcaggt	aaaagaatct	ttttatagac
25861	tttccccatt	tctttactgg	gtatgttttt	ttatttttct	tacagagtct	tgctttgtcg
25921	cccaggctgg	actacagtgg	cgcatctca	gctcactgca	aactccgcct	cctgggttca
25981	agcaattctc	ctgccttagc	ctcccagta	gtggggactg	caggcacttg	ccaccatgcc
26041	cgggtaattt	tttgtagttt	tagtagagat	gggttttcac	tgggttagcc	aggatggtct
26101	tgatctgctg	acctcatgct	cgcgccgcct	cggcctcaca	aagtgctggg	attacaggcg
26161	tgagccaccg	tgccgtggtc	cttttttaag	agatgggtct	cattatgttg	cccaggctgg
26221	agtgcagtgg	ccagacacag	gtgcaataat	agtgcactat	aacccccaaa	ctcctgggtt
26281	caaacaaccc	tctgcctca	gctgccaata	taattgggac	cacaggcacg	caccattgtg
26341	cctggctttt	ttcctttttg	atgtgaagaa	gtcttaacat	ggtaggaaaa	tcagctctcg
26401	gtgatattaa	gcagagaaaa	ggagcagtg	tagagaggta	tcttaagact	gtaggacgat
26461	ccctcctatt	tccttcagat	aaggagtatg	taaacatggt	cgtgtgctga	tggtaatgat
26521	ccagttagaca	gaggatttga	ttatgcaaga	gagagaaggg	acagctgcaa	gaacaagatt
26581	ctctgcagac	aacaaacaat	gacattcaga	atacaaatgg	aagacctggt	tttcaacagg
26641	aacaatgaca	gtgactccca	ttaaaacaca	agtgaaagtc	gagtttcggg	gtaaaaatat
26701	aattacatag	gtatatctga	aagtggaaaa	ataaggaaat	tctcttctgg	gtgcttatat

FIGURE 1-H

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26761 gaaatatgaa gtgagatcat cattcatgaa tagtagatgg caagtgaagg tttgagggga
26821 gagaaaaatt ctttagagtg ggagagtga ttagggaaat gtagtaggac tgcaggcaag
26881 agtaaggcac tatctatgat ttatggccat acgtaaaaag caSaattttg tgctttctc
26941 catggttctg ctttttagga accataaatg aaatagcaga gtttgccctg accagtggtg
27001 ggggattctg ctgcgaagaa gaagggggca aaggacttga agatgtgcaa tgaagtgaac
27061 atgagaaacc atggaatcta agctaataca aatagaaaaa ttgagacaag gggcaacaaa
27121 ataataatgt caaatgactg aagggtcaaaa tgagatggaa ttgctagaat agagggtgaat
27181 gaactgaggg ttgtagtcac acaatgggat gatcaactg gtattttaga ggtgatgaaa
27241 gttaataatt atagataaca aaatctaaag tattatctta gaagcaagta actgagttga
27301 agtggagggc aggatagtca gaaagagatg aagaaaccaa aaagtcaggg tgttgatga
27361 atcattagtg tggtttttgg acatgaccag gaatgacagc atgagtaaca gtggcaaac
27421 gacaatgggc cttcgcaacta aagtcttcag tgactacagc cagactgatg aagagaacac
27481 cagatcacca cagccaggga tagagagtaa gctgaatagc ctgacagcag ggtgactgtg
27541 caggcttcag aagaactgac aagtaaaact cacttatgta aaaaaaattt aaacacaagt
27601 gcttttcaaa aaacacaaac agattgttta tgaattgcat atgcagaagt gtacaacgaa
27661 acccacatct acagttgcct aagaagggaa gggactggaa gcaaaatatt atgatcaagt
27721 tgaaactgca aggtgaatgt cagctttttc ataatgcttt attagttcaa taacagatgg
27781 gggaaaaagt aacataatca gctgggctcg gtggctcatg cctataatcc cagcgctttg
27841 ggaggccgaa tgggggtgat catctgaggt cgggagttcg agaccagcct gaccaaacat
27901 ggagaaaccc cgtctctact aaaaatacaa aattagcagg gcgtggtggc gcatgcctgt
27961 aatcccagct actgaggcaa gagaatggct tgaatctggg aggcagagggt tgtggtgatc
28021 cgagatcacg ccactgcact ccagcctggg caacaagagc gaaactccat cttaaaaaaa
28081 aaaaacaaca taatcataat cagggcacta atactcaatt cgtggaacaa ctgtcacaat
28141 gtgcacatgg ttattagata ggcagcattt aaaataagat acttgaattg atgaataaaa
28201 tggctcatta tttaaaaaat acacaaagcc tttatataaa gtttatgtgc tagaggaagt
28261 atatgtaaga atttcaaaata agtagcaagg ttcttttctt tgacacaaaa gaagtataag
28321 acaccatccc tgtacatcag acagggttaa tactattaag gaaataattc aattatactt
28381 gagcaattaa taaatcaatg agcagataat gaagatacat tactggaggg cagtatgtag
28441 atttcaaaat gtcattgttt taactgataa tgattagtaa tataatgaat cttgacagtt
28501 ctaaaattgg aagcactgtt actttaaaaa tcaccaatat ttctaaaatt ctacaattta
28561 aaaaaggagc actcaaaagc aggttatacc cagtacgttt aagatcttta ttatttacgg
28621 gttcttcaaa cattaactca atgcaaaaga caaatacaga tttcattttt ccaccaatac
28681 aaacacatta aaaaatatac ttaaactctc tctcagctta tatattttaa aaactgaata
28741 taaaatggcc aggtgcgggtg gctcacgcct gtaatcccag cactttgaga ggccgaggca
28801 ggtggatcac ctgaggccag gagtttgaga ccagcctggc caacatggcg aaaccccgtc
28861 tctactaaaa atacaaaagt tagccagtca tgggtgcgca agcctgtaat ccctgctact
28921 aggggggctg aggcaggagg atcgcttgaa cctgggaggc ggagggtgca gtgagctgag
28981 attgcaccac tgcactccag cctgggcacac agagcgagat tctgtctcca aaaaaaaaaa
29041 aaaaaaaaaa aaaaaaaaaa aaaatatata tatatatata tatatatata tatatatata
29101 taaagtaaga aacctaataa tacgtaagta ctttaagaac aatttaatac actgcaacac
29161 aactgaactg catacaaata taagcactag aacctgaaag tacaagata aatagtatct
29221 ctccatcatg acctaaagagc aaagaaaaatc cctttaattt tagatatatt gtaaacagat
29281 gttcttcaaa gtgcaggcca tgaactagca gcaccagaaa cctcagaatt acagacatac
29341 ctgagagata ttacagttcc ataccacagc aataaagcga atattgcaat aaagcctgtc
29401 attataaatt ttttggtttc ccagtgcotg tacaagttat gtttacacta tattaagtaa
29461 ggaatagcat tatgtctaaa aatacaatgt acaggcctta atttaaaaaa actttattgc
29521 taaaaaaaaa ccgctagcaa tcactctcag cttcagcaag ttataatgtt tttgctggtg
29581 gagcatcttg ccttaataat gatagccttg atactgaggg tggtagttgc tgaagggtgg
29641 ggtgcctgtg ttaatttctt aaaataagac aaaaatgcag ttggccatat ccactgactc
29701 gttcttttac aaaagatttc cctgaagcat gtgatgctgg tttgttagca ttttaccac
29761 agtagaactt ctttcaaaac tgaagtgaat tctcttaaac cctactgctg ctttatcaac
29821 taagtttatg taatatccca aaactctttg ttgccgtttc gataatgttc acatcatctt
29881 cacctaccag gattagattc catctcaaga aaccactttc tttgattatc tataagaagc
29941 aactccttag ttgttaaagt tttatcatga ggttgacgca attcagtcac atcttcaggc
30001 tccacttcta attctagtcc tcttattatt tctaccaatt tgcagtaact tctgccacta
30061 aagttttgac ctgttccaag tcatccaaga gggctggaat caacatcttt gaaactcctg
30121 ttaatgctga tattgtgacc tcctcccatg aatcatgaat gtccttaaa gcatctagac
30181 tggtgaaatc tttgcagaag gttttcaatt tactttgcc agatccatca gcggaatcac
30241 tacctatgac agctatagct ttataaaatg tatttcttaa atagtaagac ttgaaagtca
30301 aaattattcc ttgatccatg gactacagag tggatgacaa gttagtaagc atcaaaacaa
30361 catcagttct cctgcacact gccatcatag ctcttgggca gctaggtgca ttgtctcaga
30421 gcactaatat tttgaaagga gtgttttttt tttgtttttt tctgagcagc aggtctcaat
30481 agttggctta aaatattcag taaccatgct tgtcaacaga tatgctgtca ttcaggcttt
30541 gttgcctcag ttatagagca caggtttcat tacagttata cagaacaggc agacaggctt

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FIGURE 1-I

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30601  agcataattc cttggatttt ctggactggt aaatgggcat tggcttcaac tgaaaatcac
30661  cagctgcatt agcaactaac aagaaagtca gcttgtactt tgaagctttg aagtcaggca
30721  ctgacttata ctctctagct gtgaaagtcc taaaagggtg ctttttccag tagaaggctg
30781  tttcatctac attgaaaaat tgttgtttgg tgtagccact tccattaagt atcatagcca
30841  gatcttctgg ataacttgct gcagctccta cagcagcact tggctgttta ccttgcactt
30901  tcatgttata gagatgactt ctttccctca acctcatgaa ccaacccctg ctagcctcac
30961  atttctcttc tacagcttcc tcacctctct cagccttttc agaattgaag cacagttagg
31021  gtcttgttct ggattaggct ttggtttgaa ggaatcttat ggttggtttg atctatctag
31081  accacttcaa actttgtcca caacagcaat cagattgtct tgctttctta tcattagtgt
31141  gttcactgta acagtacttt taattttctt caagaacttt tccttggcat tcacaacttg
31201  gctaactgca gcaagaggtc tagctttctc cttttattgc cattgaacat gccttccctca
31261  ctaagttaaa tctttttgac atataatgag aaatatgcaa cttttcactt gagcactcag
31321  aggtcattgt agatttatta actggcctaa tatcaatatt gttgtatctt ggggaatagg
31381  gaggcccgag gagagcgagg gagatagggg aatgactagt catcagagga gcagtacaga
31441  cacacacatt tatctattaa gcttgcgtgc ttatatgagt gtggttgtgg cactccaaaa
31501  caattaaaaat agtaacatca aagactagtg atcacatatt actgtaacag atataataat
31561  aatgaaaaaa gtttgaataa ttgcgagatt taccaaaatg tgacacagag acattaagag
31621  acatgaagtg agaacatggt gctgaagaaa aaagggtgctg ataaatttgc tcaattcagg
31681  attgccataa accttcaatt tgaataaaat gtagtctctg tgaagtcaa taaagcaaa
31741  cccaataaaa tgaggtatgc ctgtactttg cttgttaata gaatgaacgg cttgttcaag
31801  caaatttctg tgctcaagtg gaaaacttag aacaaaacaa tttcaatatt tgcaaatgtt
31861  ctttagtgac tgttacttac ataaaagttt gaaaatcctt taaatgtaac tactactata
31921  aaataataaa ggtgaaaagg atccccctt tctaattata aaaatttga cttaaagtag
31981  attttaaaaa atgagtagat taacatgctt aattgtttct ttaaaaatat ttgcataatg
32041  tttaaacttt atttactga gaacatttca ctaatggcat cacaactgaa gaagtaagat
32101  aaatttaagc aaacgtatgc taacagactt acagttgggtg atatcaggtg gtgcatagcc
32161  atcattcata tacatacttg tgggttttgc cactttcaaa taaacaaaaat cagatgtgtt
32221  ctttaaggca gttactgctt ctctcagagt tttcactgtt aaacatacgt tattcaccta
32281  aaaaaagttc caaaagacat ttatgacata ttcaactgtt ctctgagttt tggaaacaat
32341  ttcacgaaaa gaaagggaaa ataagagagt ggtttaagga aaataaaggt atgccgaaag
32401  aaaataccca tgtttgatgt ctatgatctc agtaagttgt ttatcatgac atgtgaagtc
32461  gttgaatggt aacagaatag cccatcttga ttccagtcct catacctcct attctcccag
32521  tcttgatttt ctctcattta taggcattta ggaatgtgtg tggatgcgtt ttagacattt
32581  ttatctttta agaaatgaaa acatactaaa atttttgttt ttatgttagg atttttaatg
32641  taaggtacct tagagactgt tccatgttgg gacacaaatt aatagaatta ctacattgta
32701  acaaaacagc tgcacagtag cccattgtgt ggctatatca taatttatta aagatcatat
32761  ctgttaatat tcccatattt agatttgaaa actattagaa cacaattgag cacaaatatt
32821  taaattgttc tcttaaatgg ttttagtaaa tttatactca ctaccacaga atatgagagt
32881  gccatctac ttagaccttt gccaacatta aacattatca actaatttaa aaaatctgta
32941  aaatgatgca tcttttaatt tatacatcaa ttagttttaa atttctactt tcgtaatact
33001  caagttgatt ttttttcaat tattttttgg ccattcacct atcttctgta tagaaatata
33061  actgattttt aggtagtgat gtatcctgca accaatacta aactaattta ttagtcttat
33121  tagcaggttc ctaggatagt ctatatacaa tatgatgaca tcagcaataa tagttttatt
33181  tcttcccttc tttttttttt tttttttttt tttttttgag acggagtctc gctctgtcgc
33241  ccaggctgga gtgcagtggc gggatctcag ctactgcaa gctcgcctc ccgggttcac
33301  gccattctcc tgcctcagcc tcccaagtag ctgggactac aggcgcgccgc cactacgcc
33361  ggctaatttt ttgtattttt agtagagacg gggtttcacc gtttttagccg ggatggtctc
33421  gatctcctga cctcgtgatc cgccgcctc ggctcccaa agtgctggga ttacaggcgt
33481  gagccacgc gccggccta tttcttctt tctaactga ttttctttt cttttcttt
33541  tcttattgcc ctggatagaa tctcaactat aacactgatt agaagtggta gtttatgtct
33601  ttctagcaat ctgtcaattt catctaagtt acctcaggta ttacacata gttactcata
33661  atagtctctt gttttccctt tttctatgct gctttcagaa atttcagcct tctctctttt
33721  ttcttggctg gtctgaaggt ttgtcatttt ttgtattttt ttttcaaagg accaactttc
33781  agttttgtct gtcttcttac atcttttcta ttacctattt cattaatttc tgcctaatc
33841  tttattattt ccacccttct gtttgcttta ggtttggatt gttcttctct ttgatacatt
33901  tttttttttt gcaaataagt aaaacattat caatgtttcc gttttaaatt accatgtatt
33961  aacaatatta actttaatat atttttcact ttttctaat ttgtacctt atagttgact
34021  attgcagttt ttaatatatt cacaataaaa tgtaaaggtc acagaataat aatttccctt
34081  cactgatgat taacattgct ttgcagagtc tcagcagcat ggtcattttt atggctccac
34141  attaccatgc aaagcaagga ctgcctgcat tttgaaatac atattaaata gctgtggcat
34201  actgctgaaa tacacattaa atagctgtgg catactgctg aaatacacat taaatagctg
34261  tggcatactg ctgaaatata cattaatat ctgtggcata ctgctgaaat acacattaaa
34321  tagctgtggc atactgctga aatacactgt ggcatactgc tgaatacac
34381  attaaatagc tgtggcatac tgctgaaata cacattaaat agctgtggca tactgtgaa

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FIGURE 1-J

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34441   atacacatta aatagctgtg gtatactgct gaaatacaca ttaaatagct gtggtatact
34501   gctgaaatac acattaaata gctgtggtat actgctgaaa tacacattaa atagctgtgg
34561   tatactgctg aaatacacat taaatagctg tgggtatactt ctgaaataca cattaatatg
34621   ctgtggtata ctgctgaaat acatatataa tagctgtggt atactgtttc tttggtggcc
34681   tacaataagc catgcatcct ggtattcaca cccttgtaaa aatctctttc tacactgaat
34741   tttgcttgct cacgtaacta gcttttagcca atgaggtaca gtagttgtga aggaaagaga
34801   agattgataa aaacaatgta ccagtgcctt tcttcttttg aaagcttact tttggaacct
34861   agccaccatc ctgtgtgaaa ctcaccctaa ccacgcaaag agaccactgg ataattaagc
34921   acctggctaa cagtcaccagc tgagttccca gctaagagcc aacttgccca ccataatgtg
34981   cagccaacct aacagtggat tttgtggcct agtacagcaa agacaagttg ttcttgccaa
35041   gccctatcca atctgcagaa ttgtaaacaa atacatgagt ggtgtttttt agccattaat
35101   ctctgtgttt tctcacatat cactagatac ctgacacaag agctgacaca atttgctgag
35161   ggatttaatg tgaaatgtgt aagatgatga tcccaaagtt ttacgccaga gaaaagttat
35221   ttgacctct accagagtcg tcttctacac attaagaaac agtgaccttg ggagtgaata
35281   gtaaaaagga gaaaatggac aaggagttag ttctggatta cttcaatggt tagaggttac
35341   agatatgagg aggcaccaga catcagaaag acagaatgaa gtagtgctac taagaagaga
35401   aataccaaga taaagggtga ctattaggca aatgaaaaag tgtagaagg aggaaggtgt
35461   gtcaaaactcc agccagataa gtcaattaaag atgaggactg agaattgaat gattccagtg
35521   taattaagag aacaaaagcc tcactaaaag ttgatttaag agagagactt gccacaatgg
35581   tatcagcaca ggttgctgtc tctaccacc aaagccagtt ctagagaaac cataaaggaa
35641   aacatggtag ccaagaaatt aaaaagtaaa actgagaaaa ctagtgaac agaaggctgt
35701   cttgactgtg tttgtgtgtg agtgatgagt gatggtgaga tggtagctgg tatagtttga
35761   ggaagagtg gtgactctag ctgtgaaagg ataagttaga gaaacatagt tcaagttctg
35821   ctctttcctt ttgcgcacat ttaactaaa ttactctoct tgcaacaata caagactcta
35881   aacaggatgt agaacaaagg aatcttttat atattgctga tgtaaatttt tacaagcagc
35941   ctggaaaaca acaggatggt ttttaaaaag aatgctacta gtaggataat caataatccc
36001   atgacagtca agtaaaattc ttgtacatgt tcaccagaac acacagcagc tcttcccagg
36061   aaaattattc ataataccaa aaaaaaaaaa aaaaaaaaaa gacttaaaat agatttttaa
36121   aaaccagtac ttgctagtat atttttaaaa accaacttoc tactatgcca gctccagttt
36181   atgtgccttt tcagattctg ctaggccttg gctgcttgct cagtggagag tcttgactat
36241   tatactactt tcatcttgct tctgcccctt cccagttttc tgagcctctt ctggctggga
36301   ctgggcatgg ctgatgtgtt ccacacagtg agggccataa catgtcaca acctatgttt
36361   gacctgtcat accactgcaa ctctaccatt tttgggcttg ggtgaagtgt tgtgacctgg
36421   agtataggag ctggcttccc tagaaactgc tagaacggga gttgggtaac acaatccaaa
36481   agcttgggac aaataacccc tagggggtag acaagagaca ggagaataaa agggccagca
36541   gataaacctt tctttctttt ctctggatgg ctggatgtaa ggtttatgat gcccgatgg
36601   tttttacagt gtctgcctag aagactgtta tacatgacaa gcaacaagct acctataaa
36661   attacagcca gctcagacac attctacctt ctattggctc tcgttcattc tctgcttcac
36721   tctctatttt tactactct agccttcttg agatcacaca gccaaataat accttagcac
36781   ttttagctttt cttcagattc cgtttcccta aggaacatgg actgagacag ttattgattg
36841   atatggtatg gctctgtgtc cccaccaaa tgtcatctg aattgtaatc cccatgtgtt
36901   gggggaggga cctgttagga ggtgattaga tcacggaggt gggtcccat gatgtctct
36961   tgatagttag tgagtctcat gagatgtgat tgttttataa gcatctggca tttccactgc
37021   tggcacgtct ctctcctgct ggcctgtgaa gaaggcgtg tttgctttcc cccacctcc
37081   accatgactg taagtttctt gagtctggtg agtcaattaa accgctttcc tttataaatt
37141   .accagtcctc gggtaattct tcatagcagt gtgaaaacaa actaatcac tgatgaagac
37201   tggacaaata aattgcagta cagacataca gtggaatagt atgtagagat aaaatgaatg
37261   aacttttagct ctaagcaatg atatgggtaa gtctcagtaa agcaatattg agtgaaaaaa
37321   atactggaga tgaaagtctc atacagtgca atagtgtttt gaaaaagctt caaaaacaaat
37381   aataactaac aaaattattt aggcataatg atataattaa actttttttt tttttgagat
37441   gggctttcac tctgtcaccc agactgcagt gcagtgggac aatcacagct cactgtaacc
37501   tcaacctoct gggctcaggt gatcttctca cctcagcctc ccaaggagct gggactatag
37561   gtgtatatca ccaggtctgg ttaatttctg tattttttgg agagacagg ttttgccatg
37621   ctgcccagc tggtctttaa ctctctggct caagcaatct acctacctca gcctcccaaa
37681   gtgctaagat tacagacagg tgtgagccac cacaccggc ctgattaaac aatttttaag
37741   aagcaaagga ataagaaaca caaaatggtt gatgttctaa ttcttgggct gggtaattac
37801   taggtttcat tatactatta agtgaagtaa aataaaaaag ggtcatgcat aaacaaatga
37861   tgacattggt ttataaacct aaggattatg atgaaacact ctgtgcatac agccctcaa
37921   caacaacaaa ggaataaaaag gaaaaggtag gaggagctag cagagaaaag agaaatgaca
37981   aataaagaat taccaagaat catttttttag gatttgatac agcaaggcta gtatttgcta
38041   atttaaacat catttagacc tttttggtat ggagaaattc cagtatctat cagaaaaata
38101   aacagactac aaaatgattt aaaagacaat agatttctta tacttactgc taaaagttta
38161   tctccaatct gaagtttgcc atccttatgt gctgcacctc cttcaattat tttggttaca
38221   tagatgctat tatccccagg aatatgctga tttccaacac ctccagcaat gctaaaccca

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FIGURE 1-K

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38281 agacctgttt ggaaaacagt tctagattct catccataaa tatgaactta agcccagaaa
38341 gaaatgggtt gaaactacaa ggtaattatt coctcacact aatattttttt aaaatagaaa
38401 agaattctatt tagttatcta ctagtatatg ttctgcaatc aagggaacact tagacataca
38461 gctgctccta gagttacgaa tagattccctt ttatcccaca tgttccttct tagtatctttt
38521 tcgcaaatgc acttgttatt ccaaagtgc attgcgaaat tatgtttttac ttttgtttcc
38581 atcataatta tgcttaccta cacttttaaat attttcacaa gaacaaaatt attgagaaga
38641 aataacaaca ttgtctgggtg atgggtgggca gaaccaacag gctttaaaaa tgtgaatacc
38701 tttgttcttc ttcaatatcc cactttttaa tatgaattaa caatttttaag taaggaattt ctgtaattcc
38761 taaatcccat agcttcaata tcagataaatt tctcagctct ccattcctttt ttcattttgtt
38821 gacatccctc ctcttccatg aagccacata ttgaaactac tatttccatt tatcctcaag
38881 ccatcaatgt tttaaaaatt cagcaatcac atcttaacag tcctttactg cagatgtaac
38941 tgctcataat acatattata aacacttctt cttttaactt agcctgtgta cctgcattta
39001 aagtattttg tagattatca caagttaata gcaatactaa acttcaaagt gttcaaggac
39061 acaaatattt cactctttta atgctagaag tcttcaatat aagaatactt aatacaataa
39121 gggacatatc cacttataaa acaaatagat attttgttcc ctacttttaa aaactcttaa
39181 aaacatgctg agcaaatatt gaataataaaa atcataaaaa acttataaat ttatatatat
39241 gctcactgca gtaaaatgta taaaagcata catcaataaa cgtaagaatt ttggggccagg
39301 tgcaagtggc cacacttgta ataccagcac tctgcggggc tgagggtggga gaactgcttg
39361 agcccaggag tttgagacca gcctaggcaa tgcaggggag cctcgcgtctc tacaaaaaat
39421 aaaaaaaatc agcccagtgt ggtggtgtgt gcatgcagtc caagctactt gggagggtga
39481 ggtggaggga tcgcttgagc tcaggaggct gaggtgcag taagccatga ctgcaccact
39541 ggactccagc cagggtgaca gggcaaaacc ctgcctcaaa aaaacaaaca aaaaaacccc
39601 gcaaaaaaag gaacttttca aatgctgcaa tcttggtaga aatgtaaata ttctaaaaatg
39661 ctacgtaaaga caaaaatcag tagaaaataac ggagaaatta aaatccactc aagtctgtga
39721 gaatattact aatactgtac ttggaatgta tgtcacagat aaagttcata ggtatatatta
39781 actcagagat ttcttaaaga tttatcttag tttgacttac cacatacctt taggaccttt
39841 aatgagcttt atttccatta ttttttctga cactggtttc cttcttttta catacaagcg
39901 tacaatagac cctgcttctt tcaacgcttc aactgctttg ctatgtgtta catcacgaac
39961 atctacttca tttactYgta atatacagtc attgaccctg agaaaaacaat taaatatata
40021 aaataaaaaat taaatataat ttaaataata attttccact ttaccaattt tttgttactt
40081 cttttttaag gtaaagagaa ttataaataa ttctggagta attocagaaa acataaatga
40141 agaaagtata tcaaaaacta atataaacia atacaaacat ttcccaaggg ccagcaaaag
40201 gaacaaaaaa aatagtgaaa ataataagatt atataaaaa gttaaataat aattacagct
40261 accatttgca tacttcctgc atgcttattc tgtgtaggca ttaagacaca cttataaaaa
40321 atagcaaaaca tttatttagc actaaccaca tgccaggcac tttcttggtg ttttaaccct
40381 catgacacct gtaagcttaa tatatatattt aatccctatt tcacagatgg agaactgag
40441 gcacaaagaa tgtaaataac tttcctaagg ccaccagat aataagtgc agagctgtga
40501 ttcaaaagata agaaaactga ggtcacatc acgagtttaa ggtcacagag atagtgtgaa
40561 aactgagata aagtaaaaat aattttctga gtgcctattc caacctatat attagacata
40621 aaacaattaa gttatttttt gaaatattata taaagattag gtcacttaat tcaaagggtt
40681 cgtaggtaaa gaacttatata tttgccatgg tgttatgttt tttaaaagtc tgatttgttc
40741 ctagtcttag ccttttccct agttctgtgc tctttgattg catggtattc caccagggaa
40801 aaaagatggt catctcaaat tgggttagaga gggtaaacaa aacataatta aaatatataa
40861 actggtcctg acaagcttct atattctaaca gaatcaggaa gtaaattgtc acatttacat
40921 gaatggtcaa atgatttaatt tttatatcta tttgatttca ttaatatacc acctgtcata
40981 cccagtgaga attataaagc tttagaattc aaaaactgcg taaggcatca acgtccttaa
41041 aataagatgc tgttttttaac agactacata aactctttag tcctaaaact tcagggtatt
41101 tgaacaacaa acaaggaaat aggaaaaatg acataattta tgacctcaa aaaaacaaag
41161 tttgcaaaat atatcttcca aaatggaaca ctaaatttaa acagagacaa atgttatttt
41221 catctagtca ataagaaaat atattattta aagtttgcac atagtctttg tgggtgtggga
41281 ttcWacatgg atgtgtgatc ctctatcttc cgtatcttaa ataagtttat atacatgttt
41341 cccagccaga gaggaatggg aaaatattct gtgagtgtac ttaaataagt ttatacacat
41401 gtttccagM cagagaggaa atggaaaata ttctgtgagt gtatctgaaa acacaaaggg
41461 aaactcatga tttctaYaaa tatgctcaca aagattttaa ccatcaacca aatYtgttat
41521 tcaaaatggt ataatatcta agataaaact ggagtctaaa tgaaaacagg aacacaatgc
41581 ttagagcata attatctcat tcattgactt gaatgttgtt aaagcatcta ccctatgcta
41641 gttatcatga tcgtgtttgt tatttgtatt tatcccttat ccagtctgct tcaagaaaaa
41701 tacacaaggt ggattcagca tcacaataaa aagcgcaaaa cataccgcaa tcttccactc
41761 tggggcggtg ctccccctgt gataattttg gtaatgaaaa tacttgagtc atctccaatg
41821 tgtgggttgt ccgtacctcc tgcaatgctg aaaccaagcc ctgaatttcc ctgaggatag
41881 aagaaaaaaa attgagactg aatatgattt atctttatgg acagggttcc gtcatataag
41941 gacgcagaaa ctgtactaac ataaggaaca caacaaataa aggtatatgg gtgagtaata
42001 taaagattct aaattaaatg gacttgttct ggaggaaagt cctttcagag gcattactgc
42061 tgaacagggt aggttcaaga aatacaccca aggacttttg aagtatactc cacagttcct

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FIGURE 1-L

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42121 tcttttaaag tatgtgcaac ttgtcgttgg attagtcacc catctgcaga ggtgtcactg
42181 taagtctgtt tcttttagac tgcacctcag ccatgtttgg tagggcacat ctctcctaag
42241 agacaaatgc tgaagtgatc ttcccgtgtg tatttctgag tagggcaaac ccatatactg
42301 ttttagcctt taaaaaaggg ggtggcgatg gtgcttttct tctgctaact tgacatcagc
42361 ttatttttaa atgaccaa atgtggctgct aagtgatagc tgccatcagt ccctgacatg
42421 tttaaccaat atacccgatt agcaaaagggc attgtttcac actgactgaa agaccaacct
42481 gagaacttaa cattgggtgaa ttttcttgac agcaaagtaa attttgcaa agcagctcta
42541 ctttttgctt gttttatgaa ctggagaaac aagatttctg aatatgttct tcacagaaag
42601 ggttcRactg ctacaaaaag cctttaaaaa taattgattt aaccaatggg attaaaaaat
42661 gtttattttc tgaagaatgt tctaactgaa tttcaggcaa ctcaagtaag caaatatatg
42721 tggacctatc atttaactgt tMgtattaaa cagtgtaaac acccactcta ccaccatttg
42781 tcttaaaatt ctattttaat aaaaaaaggt ttttcaatct aacttcatga attacctgaa
42841 tcttaagaac agtaccagtg gattatggga ggttaccaaa ttacttaggt actcaagttc
42901 ttcaaccagt gaaaaataca atgtatagtc ctaactaaac aaaaggaatt taaaaggccc
42961 tgggaaaaga taaaaaatca ataataaaa aagttaggag acatcacaaa ctactatatt
43021 aaagtatgta cagtacatta atactgtgct tacttgaata ttactccagt agccacccaa
43081 cttgagcaag tgatccgaat ttaagtatag ggcaataaag atatacatgt aagagactct
43141 ctcagattta ttttctcag attctattcc aatataaata aatctaatta tctaggattt
43201 cagtcttgag tatacacaca ttttagttact taagaaatct gcttgtgtga aacactagat
43261 ttccataaaa tgctagccag ataaggtggc attactatta taacatacaa taaaactga
43321 atgcagatat tcttttttct tttttttaga cagagtctca ctctgtcacc caggctagag
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43561 cctcggcctc ccaaagtgtc gggattacag gcgtgagtgc agatattctt gagggaaaaa
43621 catatcttaa gaaaatttgc acatctgaat tgcaccttca agtcatttct tgattgggca
43681 agtatccat aattagtttt taatacagct ctgtctgtta gaagtatggg tatttgccta
43741 gaaaagaaaa ttgatataat gaccatgtta ctagtatact acttacttaa tacgaacaat
43801 acttcattat catatgcata taaacaatat aaacaaaatt aaaaagcaag aaaaatctga
43861 gaaactatca caatctagag gggctctaagg cggcaggata actaaacgta atgtagtttc
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43981 aataatgtat gaatacaggt gtcttagttg aaataaatgt actctagtta tagtagtaga
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44401 gaaacttcag agtgtaaaat ccaaaatggc aaggcaaaat ttttgtatga tttattaatg
44461 aaaacctgtt gaatgcgaca gtaatcaaac acaatagctt cattttaata attctgggga
44521 agattttcaa ggaatggaaa aatacaaatg tgattaatga gttgacaaca ttcgtgggat
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44641 tctctgtctt gatccacaca tctaactcagt taccaactgt ttctgatttg aacaccttaa
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44821 cccactgcc caaatcactg ttttaaacag ctggatcttt tttgttttgt ttttttgaga
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44941 aagctccgcc tcccgggttc acaccattct cctgcctcag cctcccgagt agctgggact
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45061 accgtgttag ccaggatggg ctcgatcttc tgacctctgt atccaccgcg ctccggcctcc
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45241 ctatgggttg gtaatcatgt cttcgaatga actgaccca atgtactact tcccttcatt
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45481 tctccctcca atttatttcc tagtctctcc tgaagaaagt taactcctac agtaaaggcc
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45661 tacttctgaa gatggctcac atcttccatt ccagacattc ttttgcaata taactaaatc
45721 accctaccat caaaaggagt ctctttctct ttcaattaga tctaggcaag cctgtgtact
45781 agctttgact aaaaataatg tggcacaaat gatgtctgtg gatttctgag actaggctcat
45841 ctgatgcctg atagtattat ttgcctttgc ttggaatata ttttctttag aaccagcag
45901 ctataacatg agtaaaactc aaacagccta cagagagatc taaccaacag agaaccaaaa

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FIGURE 1-M

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45961 cccttggcca aaagcccccag ctacactcct aaccagcagt cagcaccacc aactatcagc
46021 cacgtgaata aggctatattg gacctcccaa ccttgtcaag tgccctaacc cacaccatgt
46081 aaagcagagc catccaattc attatgagaa aaaatgaact gttgttcttt taagccccta
46141 agcttcaggg tagtttgtaa tgcaatgata gataactgca agagaaataa caaacctac
46201 ataagctact ttgctttctt aaccatacta taaaatgtag cccttaattc aggtctaata
46261 tagggaccag gagtttcttc cttgagaact tttgaagccc atctctacta cccttttggg
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46381 tctcatctat agacattttc ctcttagaga ttatatgtta taaaggcatt tatatataga
46441 gagttgggat ttcactctgt taccagggt ggaatgcagt ggcataatca tagctcgttg
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46561 tacaggcaca tgccaccatg cctggctgtt tacttttgtt tttcatagag atggggctca
46621 tgttgaccag gagctcgctt gcttgctctc tctctctctc tcacacacac acacacacac
46681 acacacgtaa aatctcttta tctcagttta ggaggagtaa cttcaagagc tgtgttgatc
46741 atgtctgtgc atctagagta cgggagggtt acctacttga caggaagtcc tttgttacga
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47521 aggaggcgga ggttgacagt agctgagatt gtgctactgt actccaacct gggcaacaaa
47581 cagagtgaga cactgtctca aataaaataa taaataaata aataaaataa aataaaataa
47641 aaagaactcg acctttttta caatagctaa aggaaaataa aatacttaag aatatactta
47701 accaaggagg tgaaagacct ctacaaagaa aactacaaaa cactgctgaa agaaatcaca
47761 gatgacacaa acaaaaacac atcccgaagt catggacagg tagaatcaat actgtgaaaa
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49321 cagtatacac tgctcagatg atgggtgcac caaaatctca gaaatcacca ctaacttatt
49381 catgtaacca aacaacaccg gctccctaaa aacttactga aattaaaaaa aaaaatccaa
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49501 aaaggcatcc agaggtaaac tatctctatt tgccagtgc atgatcttgt atatagaaaa
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49681 aaaacaattc catttataac agcatcgtaa gaataaaata ctggctgggc atgatggctc
49741 acccctgaaa tcccagcact ttgggaggct gaggcgggct ggatgacttg agctcaggag

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FIGURE 1-N

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49801 ttcaagatca acctaggcaa catggtaaaa ccccatctct accaaaaata caaaaaaaaa
49861 aaaaaaatag ccagtcattg tggcacgtgt ccgtgttccc aactacatgg gaggtgagg
49921 tgggaggatc atcttgggtc tgggagggtg aggttgagat gagctgagat tgtgccaatg
49981 cactccagcc tgggtgacag agtgaaactg tctcaagaaa aaaaaaaaaa aaaaaaaaga
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50161 ctatatgggt gccaaagacca ttcaatgcgg aaagaatagt cttttcaaca aacagtgatg
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50461 cattttctaa agttttatcc acttaaaact caacaaaaat gtagcagtat atttttacc
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50581 aagatgtatt aattgtttta atttgcattt atgttattaa ctcacctttt tctacttttt
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51121 attacgaatt tctatttcaa aatttctgtt ttacaaaagg aaaaaaaat gaccaaggga
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51301 aacaggaaaag gcagaattac ttcaatgtgg ggaggaaaatg gaacttacgt aagttgggtg
51361 ttccaagcta tctgtgtga ccagtactgg gggaggattt gcctttaaga agaaattgta
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51481 aaagacttgc tatttcttaa gttataatct tatatgagct ttttatatgt taaataatat
51541 atcctttctc cagcacccaa cagaaaaaat tatgtataag cagttaaaac agatttgctt
51601 ttaagaataa aattgctatt tctgtcaaag cagccatgat tttcttaagt ttacacaga
51661 tcaccatagc tcttcataaa aacctatgaa tattctttag tgtaaccaat aactcttctc
51721 aggttgctta gaaatcattg ttttctcttc ccaaagatac agtaaagatt tcaatctttt
51781 catcaccag gagaaaattc ttccccacag tgaactgttt ttaaacaagg aaaaaaaaaa
51841 gttcatcaca gaaagaaatc aattgtaaac ttttagaaac taaaaacaca ctcttaattg
51901 aaaaacccga ttattttcag ctgcaatgac tgctttccag ttattctaga ccactcacag
51961 aattaacagt gatttattac agcaagaaaa ataagcagaa taacacacac ctagttaagt
52021 ttggattgaa aaaaaatctt ggttttctgg ttaggttaga aattattatg tatatgaaac
52081 taaagaataa aatgcaataa caaatgaaa atataataaa aatctgatgt aattcccctc
52141 aaaattcttt ctctgcata tttaaagtta tgaaagtacc aagtcacata acactttcag
52201 agaataaaaa agatgactat ctttaaaaa aacttttaga gatatgctta cacacattaa
52261 tggttctact tcaattacct gaggaattat acataaaagc tgtataaagt aacactgtaa
52321 cacaaaataa ccattttctt ccaaatgtac aggcttttaa taaaggggaa tattc aaact
52381 tcaaataaca cattattttc agcacagtac cacagctaaa tgatatgaca aaatgcttaa
52441 agacaacctt gtttcatggt taaaaaatta aacagtatgc atttgggcta catcaagcag
52501 taagttaaaa atgagtagct aatacttcat tatataataa aataaaatta aatataatca
52561 tttatgttta gtcccaccat taaataatag tctaccttgg aataattcgg tgaagtcca
52621 ctcaacaaat aaaaattgta cttataaaac tgctatttaa gcaaagctac ccaacttaca
52681 gacatttgag attttatgaa tatttcaa atactatttc ccaatgggat attgagatta
52741 ctcaaaactg tattttacgt tgctaaaaaa attaataata caacttcact ttattctgct
52801 taagcaatta cagaagaaa gggcaagaaa gaataggata tttaaagtta caaaagaaat
52861 tacattttta aaacactatg gcaagaaaag cttttgtcc ctctgccgat tttttaccaa
52921 acatgcagtg gaaaaagttg gtttttatca aaatctaatt tataccataa ttattatgtt
52981 agctgtttat cagtaccaac tcatcatcat tttatagaag ttaccttttg attctattca
53041 tttagaaagt ctgcgtaata ttgaaatata tataaacgaa atgatataag gtgttatatt
53101 tacttcaaaa taaaacaatg gaaggttggg agtaggaggg gttatgaatc aaatagaagt
53161 acacagtttg attgctgcag ctgtgtatgg gtatacatag agttcattgt actattcttt
53221 ctacatttga atatttctga aattttgc ataaaaaagt aaacaaaaaa atcaatttga
53281 gccagtgact cagtttttaa gaggttaata gctaaagtag ttgtgaaata ctctgggtca
53341 gggttgctat taagatactg gcattcagcc aagtgcagtg gctcatgcct gtaatcctag
53401 cactgtggga ggccaaggct ggtggatcac ttgaaaccag gagttcaaaa ccagtctggc
53461 caacatgggt gagcaaaatt atgtttctta agccttatta ccgatgcttg ggtcaaat
53521 ttttaggggt ttttagttcc tccttctgga atatccttgc ccttttactg ccttaccctc
53581 caatctctaa gtgaattata gagcttcact gttgtccaag ttggaactat acacaatggt

```

FIGURE 1-O

53641	atataaattt	tagtaacaga	ataagcattt	ctatagcttc	ctatgatttg	caacatattt
53701	tctttttat	tacttctcta	gagcctcaca	cagtcctcc	gggtaaagac	aggtattgct
53761	atcttttcac	agatggagaa	aatgaatttt	aataataact	gtgattttacc	tatactcaaa
53821	tgctactgag	tggtagaggg	aggtatagag	agacctagaa	ccaggtctga	gattacaggg
53881	tcacttgaac	caaggtgcaa	tgagggcttt	ttcttcatct	gaaataattt	cacgtagact
53941	ctttccaagt	cttttagttg	tagttgtttg	attttccatg	ttacctgttc	tactactcgc
54001	tgtcttggtt	aaggatccca	aagtcttttt	tttttttttt	ttttttgaga	tggagtcttg
54061	ctctgtcacc	cagggtagga	cttttttaaaa	ctcaagttta	ggccgggtgc	ggtggctcac
54121	gcctgtaatc	ccagcactct	gggaggccaa	ggcgggtgga	tcacgaggtc	aggagatcga
54181	gaccatcctg	gccccgtctc	tactaaaaat	acaaaaaaat	tagctgggct	tcgtggcagg
54241	cgctgttagt	cccagctact	tgggaggctg	aggcaggaga	atgggtgtgaa	cccaggaggt
54301	ggagcttgca	gtgagccgag	acagcaccac	tgcactccag	cctgggcaac	agagcgagac
54361	tctgtctcaa	aaaaaaaaaa	aaaaaaaaaa	aagtcaagtt	tattggctgg	gcacatggct
54421	cacccaaatt	ttaccattct	atttcatcaa	caaaggatct	tgtagtgatt	gctgctgtaa
54481	cagactgaag	cagccttaca	aagtttcaga	gggcaatatt	acatttttaa	aaatcgtggt
54541	aaaatacatt	ctaagatcca	attattttta	aataggtcaa	aatagtttag	aaaatccact
54601	tttacaatct	gcattgtatt	tctccttctc	agcattgatc	aaagtttcat	tatgttattt
54661	gtctagtgtt	tcttctcct	ctactcaatt	atgaacaagt	gctttacaag	tgtttttcca
54721	atgcaaaact	cacaaactcc	agagaattct	tcttagatcc	taatttgaga	cacattgcat
54781	tcaaagttta	atgctatgac	tgaggtgatc	actgcagggt	aaaatgattg	taaaaacaaa
54841	tgggggtggat	tctggaaaga	aggtagagta	ggaagcacca	caaactctgt	tctccacctt
54901	gaacacaatt	ttagtggcag	catgtgtctg	atgtagatgt	tttggaaact	ggagtctact
54961	gaaggctggc	gaacttcagg	aactctgtag	ttaatttcag	tgacctgcag	gcttagcaca
55021	gcagcagctc	cccacactct	atccctcagt	caactgtgta	cgcctgcac	aagccacggt
55081	gggcagagaa	aattacattc	tccaaatact	ggagatctgt	gctctgaatg	ctgcttctca
55141	tcacaaaggt	gcaaacaggc	cctggatact	gctgttccac	ctcctcctca	ttgttggaat
55201	ccccacccca	acctcccagg	ctgaactgac	ttccaggaga	ttgaaagagc	tggaggcctc
55261	cccttctctac	acaccaattc	aatttttctt	ttcccctttt	gggagccaga	cattgaagac
55321	taggacatta	aaaaccaacc	acatgtatgg	aggaaattag	aaagtcactg	tgcatgccca
55381	ggggaaggca	taggctcaga	aaatatctaa	gaagacccta	cgttttacacc	tgaggctgat
55441	ctttgatagc	ctacaacaat	cagaaaaaca	ataacaacaa	aaaaagaaaa	ccctggagaa
55501	gaaggagaat	ctgatttttca	gagttaccaa	attattaaat	tcaagtgtgc	tgtttaaata
55561	aacaagaata	agtggcttat	taaaaaaaat	ataaatcaat	ataaaactgt	ccttaaaaaa
55621	aaataaggct	gggtgtgggtg	gcttacgcct	gtaatcctag	cactttggga	ggctgaggcg
55681	ggcagatcac	aaggtcagga	gtttgagacc	agcctggcca	acatactgaa	accctgtctc
55741	tactaaaaat	acaaaaaatt	agctgggtgt	ggtggcagggt	gcctataatc	ccagctactt
55801	ggaaggctga	ggcagaagaa	tcacttgaac	ctaggagggtg	gaggttgcaa	tgagccgaga
55861	tgacaccact	gtactctagc	ctgggcaaca	gagcaagact	ctgtcaaaaa	aaacaaaaa
55921	aaaccaaaaa	accacaaaaa	cccacaaaaa	cctgatagca	aatctactag	acaaagactt
55981	tattaaagaa	ttaaaagatg	gccgggcaca	gtggctcaca	cctgtaatcc	cagcactttg
56041	ggagactgag	gtgggtggat	cactagggtca	ggagatcgag	accatcctgg	ctaacacagt
56101	gaaaccccg	ctctactaaa	actacaaaaa	attagccggg	cgtggcggga	ggtgcctgta
56161	gtcccagctc	ctcgggaggg	tgagcgagga	gaatggcggtg	aaccggggag	gcgagcgttg
56221	cagtcagccg	agatggcacc	actgcactcc	agcctgggtg	acagagccag	actctgtctc
56281	aagaaaaaaa	aaagaattaa	aagatgtgaa	caaaaagcaag	aaagtgtgtg	atgaacgaaa
56341	cggaaatatc	aatgaagaga	aataaaaaat	ataaaattca	ggaaatgaga	agtacaataa
56401	cagaaaattc	actggagaga	ttcaaaagca	tatctgagca	ggtaaaaaaa	gtagtgaaca
56461	tgagatagga	caaggggaaag	tactgagtct	gaagaacaga	aataaaagag	attcaagaaa
56521	agtgaacaga	acctaaggga	cccgtgagac	atcatcaagc	agaccaacta	atgcattgtg
56581	ggagttgcat	gagaaatgac	agataaaaga	gtagaaaaaa	tatttgaata	atagccaaaa
56641	cttctcagat	ttcatgaaac	acatgaatat	aaacatccaa	gaagctcaat	aaacaataat
56701	gaaatccaac	agactcacac	tgagacacat	tatactagaa	ctgtcaaagg	ccaaaaacaa
56761	agggagattt	ttgaaagcaa	caagagaagt	gacttgtcac	atacaacaaa	tcctcaatga
56821	gattatcagc	agacttcaca	tcagacactc	tggaggtcat	atggcagtg	gtggaataac
56881	tcactgctaa	aataagacga	aaaaaaccca	aacctgtcaa	ctaagaatcc	tatatccagc
56941	aagacagtcc	ctcaaaaatta	aggggggaaat	taagatgttc	tctgatgaac	aaaagctgag
57001	ggagtttggt	atcactagaa	ctgccctgaa	agatgtgcta	aaggtagcag	ttcaggttga
57061	aatgaaagaa	aactagacag	caactcaaa	tcatatgaag	aaataaagat	ctcagtaaa
57121	gtaaatatcat	aggtaataat	aaacactagt	tagtaatat	gtaacaatgg	ttatgtaaat
57181	ctgcttttgg	ttttccacat	gattgaagag	accattacat	tttcaaat	aaaaaaaaaa
57241	aaaacttagc	ctagccaggc	atggtggctc	acacctgtaa	tcccagcact	tcaggtggcc
57301	gaggcaggca	gagatggcct	gagcccagga	gttcaagacc	agcctgtgga	acatggtgaa
57361	accccatctc	tacaaacaaa	acaaaacagc	aacaacaaca	aaaattaacc	aggtgtggta
57421	ggcacatgcc	tgtagtcatg	gctattcagg	agactgaggg	gggagaatcg	attgggccca

FIGURE 1-P

57481	agaggttgag	gctgcagtga	gctgtgatgg	caccactgca	ctccagcctg	ggctacagaa
57541	tgagaccctg	cctataaata	aataaataaa	taagcctaata	attaataaac	aaagtcataa
57601	ttggtaaata	acgaaaatca	attattagtt	taaaagctaa	cattataaact	ttgatttgta
57661	acttcatatt	ttgtctccta	cataatttaa	gaaacgaacg	cattaaaaat	tactagtttc
57721	tgtttttggg	catacaatat	atgaagatgt	aattctgtga	catcaacaac	tgaagggggt
57781	tgggacagag	cagttaaagg	ggcagagggt	ttgtatatta	ttgcagttaa	gcttgtacaa
57841	attgagatta	gaagtgtcta	ggatgttaaa	tgtaatcccc	atggtaacca	cacaaaatat
57901	aactaaagaa	tagacacaaa	ggaacaaga	aagttaaagt	tttctactaca	aaaaattaat
57961	caaagaccaa	agaagacagt	aatgcaggaa	atgaggaaca	aaaaagctac	aaggcatata
58021	tataaagaaa	acaaatagca	aaatgacaaa	agtaagtctt	tccttaccaa	taattacttt
58081	aaatgtaaat	aaactcttca	atcaaaagac	agaaattggc	agaataaaaa	ttttaaaatg
58141	ttccaaccac	aagctgtaca	caagagactc	actgtagatc	cagagacaca	aatatgctga
58201	aactgaagga	cagaaaaggg	tatttctatg	aacagtaacc	aaaggagagc	aggagtggct
58261	gtactcataa	cagacaaaat	agactttaaa	taaaaaaaag	gttatgagac	aacaaaggta
58321	ttatacatta	ataaaaaggt	caatatagga	atgtaacaat	tacaaaaaatt	aacgcaccta
58381	atagcagacc	atcaaaatgt	taagtagcaa	aaatgagaca	gaattgaaga	aagaaatggt
58441	tctacaataa	tagctggaga	cttcaatacc	acattctcca	taatgggcag	aacaaccaga
58501	catatgataa	gtaaggaaat	agaggagatg	aacaaacaca	atataccaaa	gagacacaga
58561	actctaacaa	taacagaaca	cacattcttc	tcaagtgcac	atgggaatag	aaggaaacta
58621	tgtcaaccta	agaaaaacca	tatacaaaac	acacacagtg	aacatcatac	tcagtgggtga
58681	aagactgaaa	gcttttctct	taagataagg	agaaggcaca	gtatgtctgc	tttcaccact
58741	tgtactcaac	atgaccacta	gctgaatagt	tgaagttggt	gtcaaagcaa	ttaggcaaga
58801	aaaagaaata	aaagacatcc	aaattagaaa	ggaagaagca	aaattacttg	ttcacaaatg
58861	atatgatctt	atatgtaaaa	caccctaaa	attctacaca	aaaactgtta	gaattatttaa
58921	accaattaag	caaagtagca	ggatacaaag	tcaatacaca	aaaatcagtt	gtatttcttc
58981	taacactgaa	caatctaaaa	tggaaattaa	gaaaacaatt	ctgtttatta	tagcatcgaa
59041	aaaaacaaat	tttcagaaca	ctgagcctcc	taaatgaaga	attaacttca	tcaagaaagt
59101	aaaaaacttg	ggcaatgaaa	actataaaac	atgtatgaaa	gaaatttaaga	agacataaat
59161	aaatgggaag	ggatctgtgg	tcatagattg	gaagacttac	tattgcaaaa	atgtcaatat
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59281	agaaatagaa	taacccatcc	taaaagtcac	atagaatttc	acggtaacct	gaaagccaaa
59341	atggtaaatga	aaaagaaaaa	caaaggtggc	gggctaacac	ttcctgattc	caaaacttac
59401	tacaaagtta	cagtaaacaga	aacagctctg	tactggcatg	cagacagaca	tacagaaggg
59461	aataaaacag	aatccagaaa	taaatgccat	atacaattat	caacctacaa	tggatcatga
59521	tctaaatgta	aaacctaaaa	cttaaaactg	ttagaagaaa	acacaggcta	aaagcgagac
59581	actggaattg	tcaatgattt	cttggatatg	acacaaaagg	acagacatgt	cttgtctgta
59641	atctctgaca	agacatgaga	cccagaatac	acagaggaac	tcctaaaact	cgacgataaa
59701	accaaacacc	ctaattaaaa	aatgttcaag	gaactcatac	agacattttc	ccaaagaaga
59761	cacacacatg	gacaataagc	acatgaacag	atgtgtcaca	aatgcaaRtc	aaaactacaa
59821	tgagatgtca	cctcacaccc	actagcctgg	ctactatgaa	gaaaacagaa	aataaaaaagt
59881	gttgggtgag	atgtggagaa	attggaatcc	ttgtgcaact	tggtggaaat	ataaaattct
59941	acaactggct	ggatgcagtg	gctcatgcct	gtaatcccag	cactttggga	ggccagggca
60001	ggcggactac	ctgaagtcgg	gagttctgag	ccagttctgac	caacatggag	aaacctcgct
60061	tctactttaa	aaaaaaaaaa	aaaaaaaaaa	ttagccgggc	gtggtggcac	atgcctgtaa
60121	tcccagctac	tcgggaggct	gaggcaggag	aatcacctga	acccgggagg	tggaggctgt
60181	ggtgagccga	gattgtgccca	ttgcaactcca	gcctgggtaa	caagagcaaa	actccatttc
60241	aaaaaaaaaa	aaaaaaaaaa	aaagScaga	ggcagtatga	tgctctgctc	tggacatacc
60301	tctaaggtaa	ttactctcac	attatgctgg	agctatttgt	taaaacttgtc	tcttgacaaa
60361	acacctagta	ggcccttaga	ggacagagac	gatgtttctat	tcactttcaa	agcacatatt
60421	caaatatcaa	aaaagaccat	gcacaaaaaa	ttagctctta	aagcattttc	aacaatactt
60481	taattacatg	atagcttttc	agaactgata	gaaataaagg	tttaaaacat	ctagttttta
60541	agcagagtat	ttactctagg	gtgcaataaa	gcctctggat	ttaataggct	agtatcacag
60601	agattatgtg	tttactactcc	cagtaagaag	aactagtaac	tgctcacctac	tctgtactca
60661	gtttctatgt	ggagaaactg	aggctctcag	aagttgagta	atctccacac	catcacacgt
60721	agaaacaggt	gaagctagga	agtgggtggag	tcgggttagga	ctataaaactc	cacgtttctt
60781	ctgcaatatt	aagcagccat	taaatattac	ctttatctgt	gccactctgt	ataataagca
60841	taattctgat	ttgtagaaga	ctttcataaa	gtacaaacaa	tatgatcaat	gtgaaagtac
60901	tctgaaaagt	ataaaaagtgt	tctacaaaatc	atgaaagact	atataactttt	taaaaagttt
60961	tcattctatgt	atcttttctaa	tttgcttgac	tctcaaaactc	attttaagg	agtcagggtt
61021	gcgttacccc	ccatttttaat	agatgaaggg	ggtataaaac	tcagagaggg	taactagctt
61081	gagtggaaca	gacagactag	attctaaatc	ttttcttctg	tttttatctc	taatacatcc
61141	taacgcacat	aaatgtaaa	tagtggatct	tttaagaata	catatttcaat	taatatgttg
61201	aaattggggt	atatgttagt	atgtatttta	aattttactt	ggggacggat	attttagtcc
61261	attatttttaa	ttttataatg	tacacattgt	acttcactaa	ttagggaacac	actttattctg

FIGURE 1-Q

61321	gaaaatgagg	tgacttcatt	ggcttctcac	ataacacaac	aaaaatggta	aaactatctt
61381	tcatgaactt	ccgtagtgtg	tttaaaacct	aaagtgaagc	tatgcagaat	aaataggtct
61441	tttttgtgtg	tatcctcaat	aaatcctc	atttaaaaaa	acaaaacaaa	acttgttctt
61501	tagtttgcgtg	tctcagagaa	atatgagata	acactaaaaa	tatgggcggc	taagattatg
61561	tgccagtacc	tgacgtgcat	taagcatcct	ctccatcact	gtaaagcgcc	tcaagttagt
61621	actcctgtct	atcttcagtg	ttacagatga	gtaaatggaa	gtgcgctgtg	gttaagtga
61681	gtgtgcagtt	acacagggtt	agtggtagga	ctggaattcc	aaccccgagt	cattctgact
61741	ttaaaacgtg	tatttttata	agactatgca	agatctcaac	aattttcaaa	tgacgtggga
61801	tgctaagtta	gggttgcttg	gagtaataa	atgagagaat	tctgaatagg	aaaagacagg
61861	ctcccaaatg	aatataaaga	gactggtaca	aattctcaaa	ggattccaga	aaactatctt
61921	aacaccaaaa	aattgactga	agtgagaaga	gtaaaaataa	ctttcaattc	tattaaaaaa
61981	aaaaaaaaact	gtactaataa	actctatata	tttggaaga	tgttacatta	ttatgatgcc
62041	ataataaccc	ttaaactggt	tgctcagaat	tatatatttat	ttataaattc	aatttttttc
62101	ctgcaatata	gagagaatat	ccatttggat	tcactctattc	attgttgggt	ttatgactta
62161	atttttaatt	attttcataa	tcaaaaatta	tatagtagca	gtattattat	aatgattaca
62221	attcagtcct	attacagtaa	ggctgaagtc	attgtaacac	tgtaatttcc	cctagaatcc
62281	ttggttgat	ggatgttccc	actgacttca	cttttttagga	gaggggaagg	gcactgagat
62341	gtgaataatc	acagctgata	tatcatcttt	tccccaatgg	agcttatttt	gaaactgttt
62401	acacagcaaa	catatgttta	cccagatttt	aggctacaga	tcaataatgg	caaaaaaaa
62461	tctatgggtt	catttatatta	cactttaaat	gagatcgtga	tctttcacac	caaagatctt
62521	tattattatc	tttaatacca	ctaccattat	tttgactttg	gataactgtt	ggaagggcag
62581	ttaatgtctc	aagccacccc	ttggaagtag	taaagctttg	aaaaactaaa	aatgattaga
62641	ctctctcaca	tttggtctatt	atttttaaac	tgttacacat	aattttttta	aagtaaaatt
62701	ttacaacaga	tttacagaaa	agttgtgaag	atagcacaga	gcattcccat	atactccag
62761	atatgtttggc	tattatTTTT	acctaataaa	tgtgaagtgt	gttatctaat	caaataacat
62821	aagaatgaat	atttccaaag	aagataaata	tataacagga	aacaaagtgt	taaataaaat
62881	gatacattgg	tacaagatca	ggagtacaat	gattttttact	aacttttaga	gaataaagt
62941	ttctaagta	aaaatgttta	aaaactgttt	taagcagatt	tctaagtaca	aaggcatgaa
63001	aacaaatcta	aggttcaata	ttatgaagtt	cattgtgtcc	catttcacag	acaacctaat
63061	aaaatggcaa	atcctgactc	cacttatatt	aaatcccaa	tgtttaagtc	cctaaaacta
63121	ctaactgaag	cccaaagtaa	attaccaaat	tacaaaaaac	agctcaaaac	gttttaaaaa
63181	agaacacaaa	tgaaacatta	aaagcaaatg	aaatttttat	aaagaaaaaa	gaaactaata
63241	aaaacctgtg	gtatgggtgg	taggtgaca	gtattctcag	cagggactgg	caggacagg
63301	atcacaggga	cagtgaggag	agaggaaga	acagcttctg	ttggctaaaa	atcatcaatg
63361	acaaaaaatc	aggaaaaaca	ccaaaataaa	agggaaacac	ataacaaaaa	gctgtgccat
63421	aaagataaat	tatagttttc	agaaataact	atgcaacagg	aaaaacatta	atacattaca
63481	ctaataataa	tgagaaaata	ttctctagaa	attgttttag	aaagttatac	ccccataata
63541	attttaatga	ttctgtaata	aaatgaatgc	ctactcttta	gatgcttaaa	tcataaataa
63601	aaaagattat	cattttacaat	attccttctc	tctctgggag	ataagacact	tgcttcatag
63661	acagactgca	aaatattttt	tctagactc	agaatacatc	tcactacttt	cctctatgca
63721	ttcagaaaaac	taaaagtaat	tttattagcc	caatcaggca	gacaaagaga	gtttacaaat
63781	ccgtgataact	aacttctggt	atcaagaata	gtaataactt	gcctcaacat	gcctgtaatt
63841	aattgcaacta	acattgattg	tctattacat	gccagacata	tctggcaaaa	atgaaaaaac
63901	aacgtagaga	gaacctggta	taaaattaaac	taaaaagttc	actgttttat	ctggcttgtt
63961	attttttaaaa	ggatgaaact	ggaacacagg	aaagttgttt	agtaataaga	cccatttgc
64021	atataaataa	aatatcttat	atatgtaaga	aaaacactaa	aatcaagcag	atgaggacag
64081	cctgccttaa	caggccttaa	aacaggaaga	acaaattgcc	agactaaaaa	aagggcttat
64141	cttcattcat	aaatgcaaaa	taaaatggca	atgatctttt	ctgcctacca	aattagtcaa
64201	attaagattt	attaacaatg	tatggagtct	cttcaacaat	ggtgctgaga	caactggata
64261	tccacatgca	aaagatgaag	gtctatagac	ccccatctca	cattatata	aaaaattaac
64321	tcaaaattga	ttaacaacct	aaatatgaga	tttgaaaaa	taaaactctt	acaagagaac
64381	atagggttaa	tctttgtgac	cgtggatttg	gtaattggaac	cttagaaatc	ataaatgatg
64441	aaagaaaaaa	atcaattaga	ctctaacaga	attaaaaacct	tttgtgcacc	aaagggcatt
64501	accaagcaag	tgaaaagaca	gcctacacaa	tgggagaagg	tatttgcaaa	tcataacct
64561	gataaggggt	taatattccag	aacatttaaa	gactcttaca	acgcaacaac	acaaagagaa
64621	acaacccaat	taatgaatgt	gtgaagagct	tgaataattt	ctgcaaaaga	ggtatacaag
64681	tggccaat	gcacacgaaa	agatgctcga	catcattagt	ccttagggta	atacaataa
64741	aagctataat	gagagattac	ttcacccta	caagggaagt	gtctaattaa	aacaaaacaa
64801	aaaacaaagt	aacaagtgg	ggcaaggatg	tggagaaact	ggaactctgg	tacaatgctg
64861	gtgggaaatg	taaaatggta	cagcttctga	ggaaactttt	agtggtttct	taaaaaccaa
64921	ccatagaatc	agcatctgat	ctagcaattg	ggtaggtaaa	tatgactgg	gtaggcatat
64981	tcccaaaagt	gagagcaagg	acttgacac	ttgtatgcca	atgttcaatg	cagcatcaca
65041	cacaaacagtc	aaaaggcgga	aagaaaccac	gtgtctatca	ggagatgaac	ggatacaca
65101	aacgtgataa	tatacacaca	atgggtatga	tttttttttt	ttttttgaga	tggagtctcg

FIGURE 1-R

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65161 ctctgttgcc caggctggag tgcagtgggtg caatctcagc tcaactgtaac gtccgcctcc
65221 cgggttcaag caattctctg cctcagcctc ccaagtagct gggatgacag gcacctgcca
65281 ccatgctcag ctattttttt tttttttttt ttttttgat ttttagtaga gacagggttt
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65581 aaatattcca aaaaagcttt taaaaatgca tgaaaactgg tctctcaca ctgctgttg
65641 atatacaaat tcacacaaac tttagggaaa gtaatttggc agtaaatatc tagagcttta
65701 aaaatgtcta aacttggcca ggcacagtgg ttcacacctg taatctcagc actttgggag
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66421 gggagggtga gtcaggagaa ctgctgaac ccagcaggtg gaagtgcag tgagcagtga
66481 gtcacgcca ctgtactcca gcctggcaca cagagcaaga ctatctcaa aaaagaaaga
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66601 cagtttataa attatatggg acattgctta tgacaaaaca ttaagtaaaa aagggaagat
66661 gaaacacata aaaaaatggaa agaaatgtct gaaaaattaa tctctggggt gggatcatga
66721 gtgcctttct ctatcgctgc ttctttattc tgaattatac ttttccagtt gttgacaagg
66781 aatacacagt gccgttatta atataaatgc aaggggaagg atgggagatc attgtgtaat
66841 attaacagaa aaacaattat tatgatcttt aagtgtcatt ctctagaaaa caaactgaaa
66901 atgtatttca cactctggac tcctgttaac tggattttat atttcctgta gaaagagatt
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68761 agcccatact gatataaata aatacatcaa taaataaatg aagataagag cattttctta
68821 caacaaaatg ctaactaaaa atgtaattat ggaattataa aatcatcatt tggcagccat
68881 catagtaata tagtaattca ttcaagaat attaatgaat attaaaactt cctgttgcca
68941 agtgaaacgt ccattccagt ggtatgaatg gatatactca taaaaaagtg tctcctttca

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FIGURE 1-S

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69121 caatacttcc aggatatttc taccaaagggt atataacttg aatctaataca ttaaacaatca
69181 gacaaaccca aattgagtga tacattacaa agtaactagc tgcagtcac tcaaaagtgtca
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69361 gcacataggc atacatctat gaagccactg ccataatcaa agtaacaaac gtatctatca
69421 cctctaaaaa cttccttgtg cctctgttgt tttttgtttt gggttggttc ttttaaggac
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72601 atcaactgtc gtgtcactgt ggggttagtaa ggatcttatt ttgggtttgt atggcataat
72661 taatattcct aatctaagtt ctttggttct ttgtttaaag atgtattatg ctgtaatgtg
72721 gcatgtttct ctgattaaat gtcaaagaag ctattttaaa gtaagagaga aactaaaaaa
72781 aactgcaagc cttttgaaatg tttatagaag gataaaatat agcacagtag atttataaaa

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FIGURE 1-T

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72841 actctgctta ggaatcactg tactcaacgg gggcccagta ccttcagaaa aagctgattt
72901 ttatggttta aatctgtttt ttatttcaaa tgtccttttg tctgtgcact gcaaacaggt
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73141 acagatctag caattaattc cattacagaa acatgagtac aagtgtgtta gttcacacag
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76381 cttgaacgtg gctgttaaaa aaaaattaac aaataattaa acaccaRgtt ataatcccca
76441 attctttttc tcagaacaac aaaacaacac aaattgtaaa gcaatcattt gggtccactc
76501 tgtcacagct gtaacttctt cacatttcaa agctgctcca gtcaagaagt cagagttttg
76561 atttcacaga tactgaaaat actgttcaga aatgctacca

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FIGURE 2-A

>7:10710001-10808300

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1      cagattcaag ttgcctgaa tatactccaa caagcagtag ttacaagtgg attttaaaaa
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121    ggtatacatg tgccatggtg gtttgctgca cccatcaact cgtcatttac attaggattt
181    tctcccaaca ctatcccttc Yccagcacc ccccccccta caggcctcag tgtgagatgt
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301    ggtgttttgt tttctgtcct tgtgatagtt tgctgagaat gatggttcca acttcatcca
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1081   cattgctttt ggtgttttag tcatgaagtc tttgccatg cctgggtcct gaatggtatt
1141   gccatgtttt tcttctaagg tttttatggt ttttagtggt acatttaagt ctttaatcca
1201   tcttgagtta attttttgtt aagtgaagg acaggtcca gtatcagctt tctacatatg
1261   gctagccagt ttcccagca acatttatta aatagggaat ctttttcca ttgctgtttt
1321   ttgtcagggt ttgtcaaagt cagatgggtg tagatgatg gtgttatttc tgaggcttct
1381   gttctgttcc atttgtctat ttatctgttt tggtagcagt accaagctgt tttggttact
1441   gtaggcttgt ggtatagtct gaagtcagg atgcctccat gtttgttctt tttgcttagg
1501   attgtcttgg ctatgcgggc tgttttttgt gccatatgaa atttaaagta gctttttcca
1561   attctgtgaa aaaaatcagt gtagctttta tggggatagc attgaatcta taaattactt
1621   tgggcagtat ggccattttc acaatattga ttcttcctat ccattgagcat ggaatgttct
1681   tccatttggt ttgtgtcctt tttattttgt tgagcagtg tttgtagttc tccatgaaga
1741   ggtccttcac atcccctgtg agttgcattc ctaggatatt tattctcttt gtagtaattg
1801   tgaacgggag ttcaacttgt atttggatct ctgtttttct gttcttggtg tataggaatg
1861   cttgtcattt ttgcaccttg atttgtatc ctgagacttt gctgaagttg cttgtcagca
1921   aacttcagcc caaaaggaga ttttgggctg agatgatggg gttttctaaa tatacaatca
1981   tgtcatctgc aaacaggggc aatttgactt cctcttttcc taattgaata ccttttattg
2041   ctttctcttg cctgattgcc ctggccagaa ctttcaatac tatgttgaat aggagaggtg
2101   agagagggca tcttgtgtt gtgcagcttt tcaaagggaa tgcttccagt ttttgcctat
2161   tcagtatgat attgggtgtg agttgtcat aaatggcttt tattattttg agatatgttc
2221   catcaatacc tagtttactg agaattttta gcatgaaagg ctgttgaatt ttgtcagcct
2281   tttctgcatc tattgagata atcatgtggt ttttgccatt gggtctgttt atgtgatgga
2341   ttatgtttat tgatttgtgt atgttgaacc agccttgcatt cccagggatg aagccaactt
2401   gatcatgggt gataagcttt tcaatgtgct gctggattca gtttgcaggt atattattga
2461   ggatttttgc atcaatgttc attggggata ttggcctgca attccttttg ttgtatctct
2521   gccaggcttt ggtatcagga tgatgctggc ctcataaaat gagttaggga ggattccctc
2581   tttttctatt gattggaata gtttcagaag gaatggtacc agctcctctt tgtacctctg
2641   gtagaatttg gctgtgaatc tgtctggtcc tggacttttt tttggttggg agcttattaa
2701   ttatttgtgt aatttcagaa cctgttattg gtctattcag agattcaact tcttcttggt
2761   ttagtcttgg gaggggtatg tttccaggaa tgtatccatt tcttctagat tttctagtgt
2821   atttgcacag aggtgtttat agtattctct gatggtagtt tatatttctg tgggatcagc
2881   ggtgatattc cttttataat tttttattgc atctatttga ttcttccctc ttttcttctt
2941   tattaatctt gctagcagtc tatctatttt gttgatcttt taaaaaaaca gctcctggat
3001   tcatgtattt ttttcttgaa gagttttttg tgtctctatc ttcttcagtt ctgctctgat
3061   cttagtattt tcttgtcttc tgtagctttt tgagtgtgtt tgctctgtct tctctagttc
3121   ttttaattgt gatgttaggg tgtcgatatt agatcttttc tgctttctct tgtgggcatt
3181   taggggttaca aatttccctc tacacactgc tttaaatgtg tcccagagat tctgcttca
3241   tgtgtctttg ttcttatttg tttcaaagaa catctttatt tctgcttca ttttgttatt
3301   taccagtagt tcattcaggg gcaagttggt cagtcctcat gtagttgttt tgagttagtt
3361   tcttaatcct gagttctaag ttgattgcag tgtggtctga gagacagttt gttgtgattt
3421   ctattctttt acatttgctg aggagtgttt tacttgcaat tatgtgttca atttagaata
3481   agtgcaatgt ggtgctgaga agaattgata ttctgttgat ttggggtggg gagttctgta
3541   gatgtgtttt aggtttgctt ggtgcagagc tgagtccaag tcctggttat ccttgttaat
3601   tttctgtctc cttgatctgt ttaatatgta cagtgcggtg ttaaagcttt gcattattat
3661   tgtgtaggac tctaagcttc tttgtaggtc tctaaggact tgctttatga atctgggtgc

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FIGURE 2-B

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3721   tcctgtattg tgtgcatata tatttaggac agttagctct tcttgttgaa ttgatccctt
3781   taccgttatg taatggcctt ctttgtctct tttgatcttt gttggtttaa agtctgtctt
3841   atgagagaca aggattgcaa cccctgcttt ttttttcttt tccatttgct tggtagatct
3901   tcctccatcc ctttattttg agcctatgtg tgtctttgca aatgagatgg gtctcctgaa
3961   tacagcacac tgataggctt tgactcttta tccaattttc cagtctgtgt tttttaattg
4021   gggcatttag cccatttaca tgttggctaa tattgttatg tgtgaatgtg atcctgtcat
4081   tatgatgcta gctggttatt tcacctgtta gttgatgcag tttcttcata ctgtcgatgg
4141   tgtttaccat ttggcatgtt tttgcagtgg cttgtatcag ttattccttt ccatgtttag
4201   tgcttccttc aggagctctg gtaatgcagg cctgggtggg acaaaatctc tcagcatttg
4261   cttctctgta aataatttta tttctccttc acttatgaag cttagtttgg ctggatatga
4321   aattctgggt tgaatttct tttctttaag aatgttgact attggccccc actatcttct
4381   ggcttgtagt gtttctgttg agagatccac tcttggtctg atgggcttcc ctttgtgggt
4441   aaccagacct ttctctctgg ctgcccttaa ctttttttcc ctttatttca acctgggtga
4501   atctgacaat tatgtgtctt ggggttgctc ttctcaagga gtatctttgt ggtgttctct
4561   gtatttctctg aatttgaatg ttggcctgtc ttgccagggt ggggaagatc tctgaataa
4621   aattctgaag agtgttttct aacttgggtc cattctcccc atcactctca aatacaccaa
4681   tcaaacatag atttggctct ttcacatagt tcttgagggc tttgttcatt tcttttcact
4741   ctttttcttc taatcttctc ttctctattt taaccatttg atctacaatc gctgatattc
4801   ttcttctctg ttgatcgaat tggttattga agcttgtgta tgcttcacgc agttcttctg
4861   ctgtgggttt cagctccatt aggtcattta agctcttctc tacactgggt attctagtta
4921   gccattcatc taaccttttt tctagggttc taccttcttt gcgatgggtt agaacatgct
4981   ccttttagctc ggagaagttt gttattaccg accttctgaa gcctttttct gtcaactctc
5041   aaactcatte tccatccagt tttataacct tgctggagag gagctgtgtt ctttggagg
5101   agaagagggt ttctggcttt tggaaatttc agcctttttg ctgtgggttc tctcatctt
5161   agtgggttta tcttcttttg tctttgatgt tggtagaccta cggatgtggt tttgggtgtg
5221   atgtcctttt tgttgatgtt gatgctatct ctttctgttc ttattttacc ttctaacaga
5281   caggcccttc agctgcagggt ctgctggagg ttgctggagg tctctccag accttgtttg
5341   cctgggtatc accagcggag gctgcagaac agcaaatatt gctgactgat ctttctcta
5401   gaagctttgt cccagagggt caccacctg tatgagggtg ctatcggccc ctactgggag
5461   atgtctccca gtcaggctac tggggggtca gggaccact tgaggaggcc gtctgtctgt
5521   taatggatct ctaacaccat gctgggggaa ccactgctct cttcagagct gtcaggcagg
5581   atgtttaagt ctgtagaagt tgtctgctgc tgccttttgt tcagatatgc cctgccttaa
5641   gaggtggaat ctagagagggt agtaggcatt gttgagctgt ggtgggctct gctgattctg
5701   agcctccctg cctctttgtt tacactgtga gcatagaact gcctactcaa gtctcagcaa
5761   tgggtggactc ctttcccccc accatgctcc agcgtcccag gttgatctca gactgctgca
5821   ctagcaacga gcaaggctct gtgtgtgttg gccttgccga gccaggcacg ggagggaatc
5881   ccctggtctg cctgctgtga agactgtggg aaaagtgcag tatttgggca ggagtgtaca
5941   gttcctccag gtacagtcat tcacagcttc cttgttttag aaaagggaat tctctgacc
6001   ccttgagctt tctgggtgag gtgacacccc accctgcttt ggcttgtcct ccatgggctg
6061   caccactgtt ccaaccagtt ccagtgggat gaaccaggt cctcagttgg aaatgcagaa
6121   atcacccatc ttctgcatcg atcttgacag gagctgtaga ccggagctgt ttctattggg
6181   ccactcttga agtgcccccc aaggagcttt attgagagac agaacagctc tcagtgaaag
6241   ggagacccaa aataacctag cctccctctc aggcaggtag tctgaaatg tgtctgagtc
6301   tggctgagtc tgaggttttt atgggctcag aatgtagaaa gtgcatgctg attggtctat
6361   ggggtggccc agaaaaagca ccatctgatt ggccRaaagg catcaaagaa cttctcactc
6421   ctggtcatgg actctaccca gaacaggtag cctggcccac aggcttcagg ccatccctgg
6481   cttgaagggtt ggtcctcact ggggacctac ctttcccg ctaggaacct gtctgcctcc
6541   caccaccatc aaaaccttga aagcccatct aattgggtga atctaaatca tatctataat
6601   cctagtttta agtgagtctg agaaacgtag tttttattct aacatgatct gtaatacaga
6661   ggaagagggtg agaataaag tcacctgcta gtggacaata tctagcccaa ttttatgctt
6721   tgtctactca gcaaccagat acacccttct atccgtaaac ctccccacaa tcacaatagc
6781   aataaaacca ctaccaccaa acataaggta actcttctta atatagatga aaacactgtc
6841   tccttcagggt tcagaatttg tccttggccc ttogaacata ctgggatctg attccattta
6901   tagggatgca gtgagagaga tgggcatgag gagaatcagc atccctttgc aaagtaatga
6961   actcagttga gtccattcat tacagtgtct tcaacaaggc aggtagcttc accaagaaag
7021   aagggtctaa ttctactaag aaaatgatgc tctgagattt tgaggcttgg ttttcaattc
7081   tcaaggtagc attctatccc aataaataat ctaaattctt acaaagttgc ctaaaacctg
7141   caacttgtgt attcagattt atcaattgtt aatgatatca gtccatgat gacatgggat
7201   gaaatttaatt tagagtagta gttttcattg gagggctgag tgatgggtgt gccactgttg
7261   ttggtagtga tttggctccc cagtggatat ttggcaatgt atgtccattt tgagttgtca
7321   caatttgggt tagggagagc tgttagtggc atctagtgga tagagtccag aggtactgag
7381   atatcctaca atgcatagga cagccttctt cagccttttg ccacagggcc aaagaattat
7441   ctggcccatc aataaggaca aagataagaa atcacagaag ctctctgtgt gttggaacaa
7501   gttttgagtc aagcagttaa cgtcagctgg atgtagtac tcacacctgt acccccagca

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FIGURE 2-C

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7561 ctttgagagg ctgaggcagg aggatcagtt gagctcagga gttcaagccc agccttggca
7621 acgtagcgag gtcccatgtc acatttagaa atttttttaa aaagttaaaa ccctgggctt
7681 gtcacatttg ttctctaatt ttccaaggc tgtcagaact gccacctcag cccaccccag
7741 tccatttatt gcttattttgc attttagtgt tctatcataa caacaattg ctaacagatc
7801 ttgtgttcaa caggcacctt atttcagttg atgacatatg ataatttaag taaatgtatt
7861 accactgcat gtcttggact accaatatct tattttccac tggtaatcaa gatatcattg
7921 cctttaaatc caaactgggt caaataataa atatcaaatt ccagtggttg aagttttatt
7981 tctttatfff ttgaacatct ttatatacca actattgtat cagacaaaat tagtatagca
8041 aatagaaaac actacatata tttcatgtag aaaaatattt tggtatgtat aaaaatcattt
8101 aaaagactga aggagtgaag gtcagagatt caaggaaatt ttcagtttca agatcatata
8161 actgtagcta tgatctggag gtcagaaaac tagtgcagct gttgctgcta accctctcca
8221 caactgctcc tccatcttgc ccttatacct ttgaattaa gtagtgaata tggattctat
8281 tcttatagat gattgagctt cttttctgct gttacagcta cacgaacatg gcctctgcct
8341 cccttacatt ttctacatat caagatgccc atgggatacc taatacatct gagttaagta
8401 attgtttaaa gtttttaaaa atttggtttc tccaatggtg ttagttttat ttaaatattt
8461 aatgattctt gggtgtctat atatatattgt gttcatagta tataatacgt agtggtgatg
8521 gccagaattg atgtactttg tccaaataag aagccctRtt caccctggcag agaataaatg
8581 caagttttca ttataggtat actggttctg atgggttgtt gtttgtttgt aggggtgagg
8641 aagttggtag tataggagg ttacatgtga gtaggctctt ctttatgatt tatgagtatg
8701 ttctatgctg gatcttccta tttcagctat taagacaact gaaagtcagt gaggttacta
8761 tcagtctcct tctataaaac ctgttttcca ttctggtaat ctctgaagtt agacttcccc
8821 cttagtagag ctgtatttga agttttattc aggagagaaa tgctattttc agctcctctg
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8941 tctcagccct tctcacacc ctcatgtctt cttacctaa gttatgcag agaattattt
9001 ggaaaaactc acttttagtg ttcttctctt tgatgattca tcacctggat gaattatta
9061 gctccttagt ctgttggatt ttgttggcaa tgtggacctt cttccagAAC tgtcaaaatt
9121 cctccatagc cctcaaaagt ctgctgggtga cattactctc aggtttatag caatgctatg
9181 attttatgga tttatttcta tttgtatatt tcttctgtga tttctgtgta ttttggggag
9241 ggtagttagg taattcacaa gttcaattag ttaattagtt tgtgaaccag cactattatc
9301 cttagattta cagcaaaacta attttacttt cttggtttct taaaaaatta atcaggatct
9361 gcagtttctc tctcaacaaa ataagacaat tcattttttt cttcatttat cttattttac
9421 tttccctaRg cacttcatct ctttaccctc tacatcttgg atttggttac cgtaatttag
9481 aattatgacc cctctagttt gcatattcct gcttaataaa actgtattaa atcccacaat
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9661 tggaaatagg gtacactgtt atctgcttct caaaacttta agtaaccaga caggttatta
9721 atattatttc cagattcttg gtgatgaatc agaggctcaa tgttgccctt ttttagggta
9781 acacaaatc agtgggcaag cctagaccMa aattcggatc tccagactct taagtttgct
9841 gtcttttgta tacatatttg tttcttttct ttacagtagg tgtccacaac aagctattta
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9961 tcataattat tactgatgct tgtgcagtca tatttagttt gcttaattag acagaattgt
10021 ggacattaag aatattattt ggcaaaatcc tacattgagg cagtttggtg tYgctgtttt
10081 ttggaaatga taattattat ataattcttc ttctttgtgt agtcatgcat aaatatcttg
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10381 aaacttagcc agggatggta gcaggcatct gtaatcccag ttaccaggga ggctgaggca
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10501 cactccagcc Rgggcaacaa agcaatactc catcccccta cagctcccc aaaaaattct
10561 gagttaagaa tgccaagagt aatttatcac atacgcctta aagatgttca gcagaatatt
10621 attggagatg ctattatagc cagtttacaa ccaataaaga caaattcttt atatgacatc
10681 aaaaatgtaat ttcctttata aatatgggtg caaaaatcaa caaaatacta gcaaaactgaa
10741 tctagcatct ataaaaagat ttatacaaca tgactaagta gaatttatac tagaagtga
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10861 gtacaaaaat cacatgatca tctcaataga cagagaaaga gtatttaata aaattcgaag
10921 ctctttcatg ataaaaacag ttggcaaaact aggaacagga aagttccctc acctgaaaaa
10981 gggcatcttt gaaaaactat agataacata agactaagtg gaagactgaa agttttcttc
11041 ctaagtcctg aaacaagaca aagaagtctt tccctacca catttattca acaatgttct
11101 gcaggttcta ggcagagcaa ttaggcaaga aaaagcaata acaagcattc acaaaaggga
11161 gggaaaagtt caagcccctt catttaatat catttcttgg aagttgcacg tactgtttct
11221 gctgacatgc aattggccag aacttaactg cataactcca agcaacatca agaaagttgg
11281 tatattatgt ctttattctt tgaaaactta tgcccagttt aaatttggag cttccatttt
11341 tgaagaaaaa ggagataatg ggtattggga aacaaccagc agttctttcc atgtttattg

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FIGURE 2-D

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11401 aatgcaggtc aaaaaaagga attaggtaat ttttttcttt tctttttacc ctacttttct
11461 tcttcccttt tccctccctc tcttcccttc ctccttttct ccttctttcc ttctcttact
11521 ttctttcaat acatgaattg caaaagatta ataacStaãa tgcaatattg tcttctggat
11581 tggatcttgg aacagaaaaa aggacattag taggaaaatt agtgaaatat aaataaagtg
11641 tttagtcaac aaaactgtac tcatgttagt ttcttagttt tgataaatgt attatggtta
11701 tataagatac tgatattagt ggtagctagg tgaaggatgt acaaaaaactc agtattatta
11761 ttgcactttt tggtaaatct gaaattactt caaaattaaa agttaaaaaa aaatgattgc
11821 tgatatccaa tggccacagg tttggaaaac tagaaagaat tcttatccac tcttgggtgg
11881 atatatatta gtacagactt tttttttttt ttttttgaga cggagtttct ctctgttcac
11941 ccaggctgga atgcagtggc gtgatctctg ctcactgcaa cctctgcctc ccaggttcaa
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12301 acgaatgcca gattttgaat ttctctttta gatgattcag cataattgct ccaaataaat
12361 ctaaaaggct attgtcaaac agtggaatat ttggatttat aatttcatag ataagactat
12421 cagtccatga tatggttggg gtttaaagta gaatggaagt gaaattccca gagtggagtt
12481 tttaaaataa ccaagttcct aggattttta ctggaagaat aaatatctga aaggcattga
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12601 gtggttttca tttgagaggg ctgcagggta actgtttcta tttcagatga ggaggtaaaa
12661 agaatgggca ttgaaaagga aaaatgttta ctaagtaggt tatacatttt ggaatagaag
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12781 tgaggcagga gaatagggtg tggaggcagg gaacctaaag atgtgtcact ccgacttctc
12841 aagaactaaa ttgaaaggaa acccctaact ttccatgcct aagtaacaaa aggaccagag
12901 gctactccct ttgcaaacc cactttttt tgcaaggcag atgggaaatt ggctgtgggc
12961 agcaaatacag actgattgca ggagagtctt cctttgcata gaagtatcac tttgtaactt
13021 caccatctgc aagaaatcaa actgattgca ggggaaatct tcctttgcat agaggatatac
13081 cactttgtta cttacccta cctctgattt gattgctttt tgcaccaatg tttgcacagg
13141 agcatgacct ttgtaacttc acttcagcct ctggttggct gctttctgca accaatcaga
13201 ctgattgcgc gttacttcat ttacatgagg tgagcattag gtggccaata ggaagcttct
13261 agagggtatt tggactcaag attctgtatc cgggcccttg agcgcgtgct caggctcgctt
13321 ccgtacagag cgtgctttaa ttttcaataa gtccctgctt ttgttgtttt gttgcttcat
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13621 ggagcctttg gggtttatgg gcggaattgc acagggttg gcgggagct ctgctccgc
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13861 gtcgctgctt tccctattgt ctgaggcagc cgccctcgcg ctgtgcaatt tctggctttt
13921 cgttgcctct ggtccaggct ataaagaatt tcttttcttt aatttttttt ctcttagttt
13981 taacgggaga aattaactcc ccggggcgcg cgggttgact gcgctgcctg ggccggaggt
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14341 agtcagggcc ggtgggagca gggcaggggg gggagagtcc tgcgggaaag caggattggg
14401 ggaccctcgc cctccatggg ccgcgggaat gaagcccgct tgttttatcc cctgattttt
14461 gccgttttta ttgactgtta cgatgtctaa gtgggggatt acgaggaagg tgcagaaaca
14521 tctcgaaaag atgagcaaga gggctcagct cgattttagc tggctctagc tggcgttggc
14581 agcatcaggg ctggaactgc ctttgaactt gccgctggag ctgtccagcc cccccacc
14641 tgcttctgca ccccaacctt ctctgaccc cttttgctga gaactcagtt agacaaaaat
14701 tccttgtgcg aggtcatctt tatgttctct tagcaccaca actctcccct gtgtttgggtg
14761 tgattatgaa tgacaatgta attttttctt cttcacagtg gatcgagct ccaagaggag
14821 gcaggtgaag cctttggcag cttctctgct ggaagctctt gattatgata gttcagatga
14881 cagtgttttt aaagtggag atgcctcagg taaatatttc cttctctctt cccctttccc
14941 agctttctgg agttaggctt attttttagc tttttaaatc ggttttgatt aaaatgccaa
15001 ttttaagtga aagcacgtaa acttcattta ttttgtccat ttgatttccc attttgcctt
15061 tagatcctgt cactagacct ataattgctt ctgttttctt cagagataat tagcagtcag
15121 ggaaggact ttttcaaag atgcaaaagg atttctctgt tttacacctt aaaatatatt
15181 tatgcttata ttatagagga aaaaactgaa agatatcccg aagtagaaaa gtatcctgag

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FIGURE 2-E

15241	aggtgtgtgg	accattaata	gtccctgagc	aggggtcttc	ttttttcaga	tcacttgaca
15301	atctcttagg	ggagttttgc	tttttttgtg	tattagctct	tttactagaa	taaaattgac
15361	cagagtaaga	ggtgcacttc	aaattatagt	aggtgctgga	ccttgtggat	tgggcctttc
15421	agatgtctct	gaagtataag	tcatgcatgc	ttgtcacta	tatttagtaa	ttttaaaaac
15481	tttttttaaa	ggtcgtatat	tcacattgta	ctaaactgga	aaacagaaaa	gtatgatttt
15541	cctttgtatt	ttctgttcag	tgtaccttat	gtatatatac	agtttcaatt	gaaggaatct
15601	gagaaacaaa	aattatgttt	aattttaaag	ttttatggga	aaaatactga	taaacatgaa
15661	caatgaaaa	tatgtgtaat	tccacctctt	ttgaaaaatt	taataaagt	agatgaaaa
15721	ttaaaataaaa	tgagaagtaa	aagcctttcc	agtttcatct	cttcaacagt	ttttaaatat
15781	acttccagag	agtttgccgt	ggttagtcac	atctctcctt	ccttctggtt	tcccttgtct
15841	ttttcctgct	agggatagta	ggaagggatg	aacgaaatta	tattactgtt	gctactttta
15901	gtagcatcaa	cagcagaatt	tgcatgtgta	tttactgata	actttttgtt	tgcataatct
15961	cacttaattt	tcacagtaac	ttagtgaagg	agataccatt	ttacaggtaa	caggggtatt
16021	gagtttaaa	aactggcatg	aggtcactca	ggcagtaacg	gatccaatgg	atttgacttc
16081	agaatttagt	ctgtttatct	gcttggatcc	caagagttga	tggacggaat	cttaaacaga
16141	aactgactat	ttggttacta	attgaattca	tccgcagcaa	tcaaaaattg	ataagtttat
16201	cttgattaac	tgttttttta	tcctttgctt	ctcagctctt	tatctcccat	ttagttgggt
16261	tgctgatatt	tggatatttc	aaagaaggga	aggggaagg	aaaggaggta	aaatttaaat
16321	cttagttctc	ttggttaaaga	ccttggcaga	taagaatatt	cctggctagg	atgtagtttt
16381	ggtttgttat	ggttgtgggt	gtaaaacttt	acaaacatag	ttgggtcgtg	gaagttacga
16441	attctttgaa	tatgggaaca	attctaaaac	ttacattaag	tattacatta	ttatgtgaca
16501	ataaatcttg	actttatgga	caatttgttt	ccaaggtttg	ttcattgaga	tggaaatattc
16561	acaggtatca	cttctttttc	aagtggtaaa	acaatctgat	acaaacataa	agtactttct
16621	caaaaatttt	tatgatatcg	agctaagtag	agatttctga	ccttggttaa	toctaatttt
16681	agttgaagag	aactgttatt	tgtgaaaaat	gataggatga	gttttgttag	gttgatatat
16741	ctatatatcc	cttaaacaca	ctaaaaatat	ttactttctg	ttccctcttg	taatataata
16801	tctagtatgc	tgcactcata	atttaccctt	ctggccctct	ggggagctta	aatttgYgat
16861	ctgtggctct	aggtcacaaa	ttgtatgta	tagttcttgg	tatttattgt	aaaagggat
16921	ttagaagaaa	atgattgtat	ttaaaattgat	Yagtagtcaa	cagaaattga	atcataattt
16981	tgactcttgt	tttaggtgca	ttgatgctct	gcatagctga	gatattSgct	tactctagat
17041	taccattggt	ttccatttga	atctttctct	tgcctgagat	agtatatatt	tagttggagt
17101	cttgtagaga	ataagacatt	agtcctatca	ctggtttcca	aacatgttga	agttgtggat
17161	tccagccct	acttacRaat	aggagattaa	attggaagta	gagaaatggt	agctaaacat
17221	ctgtctgac	atatcttctt	tcaaaacaac	ttctagaaat	gactcattga	atgaactacg
17281	gacttccctt	gaacttaata	ttaaagtgg	tagattcgtt	ggccttaatt	ttggctaact
17341	ggattccgtg	gatcaatttc	ttcttacctt	catcttgaaa	tctgaaattc	tgactataaa
17401	actttttata	tttctgtttg	gttttaagaa	taaatataga	aaacatttgc	agataaacat
17461	aatttaactc	tatcataaaa	tagaacaaca	tcaacattgg	taaagaatga	cccaccata
17521	agattggcaa	gtgattacga	gctgtacct	ttagaaaatt	atgaaactga	agatagttta
17581	tattttattt	ttaatgcaaa	agcaaaagta	agctKctcat	ttttgattga	aagcagtcaa
17641	taaagtttga	aatgagtaag	tcctaaaata	ggatatatat	gcattattag	aattatggtg
17701	ataaccacca	gaagaaccat	atgtagaana	gttaggttga	actatatgga	attaccagtt
17761	ttgtaggctc	aaaacacaca	gtcaaatatt	agcaatttca	tggttttacc	tagttaaagt
17821	gttgatatatt	gagacttggg	cataggggtg	ggtgtatgat	aggagactta	tttacatttg
17881	gttatctgct	acattaattg	aatgttttaa	agaatgttta	catcttttta	aagatgcaga
17941	catgtattaS	ttctattaac	cagacagatt	agccatgctc	tctaccctta	tccccacca
18001	ggcaaagtta	aatgggggtta	acttttagatc	ttgatcaaaa	gttagtttag	ttaggccata
18061	ttgcaggaa	ataatttaat	gagaagtgtc	agcctgagac	tttgggtgta	ttttgtgctt
18121	aatctgactt	tgaataagt	gaccaagatg	tgttcattga	ttgtccgtag	tttagcctt
18181	tgctagatgt	tatggtgaat	ttacaaaaca	gtagtaataa	tattagaata	agtaagtaaa
18241	ataacatgta	agtaaaaata	aaattagaat	aattaaataa	aatagttgat	acaaaggatg
18301	gttgatcact	tgtgtagttc	aagtctttMa	taggaaatga	gattagattg	atgtagaaca
18361	atttcattga	ggagaggagg	taaRagtgga	actatgaaca	gaaggattta	gataaacagc
18421	aatcttgggt	agggcaaaaat	taaaagtgtt	gagacttggg	attgtttttt	tatatgtggg
18481	gatcagtggt	gagtaaaagt	agaagagata	agcctggaaa	aatagaataa	gggtcaaattg
18541	tggctgtata	tacgagttta	Yggtttctca	accttggcRc	tattggcatt	ttgtgttgga
18601	taattttttg	ttgtggaggc	ttgtcctgta	cccagtagga	tgttttagcaa	caacaacctt
18661	ttcctctact	agatgccagt	agcatctttc	ctacctgccc	cagcctcacc	tccacctcca
18721	cttccactgt	tgtggcaact	attgtttcca	gacattgcca	gttgtcctct	gggggaaaaa
18781	aatgttcccc	tttgagtacc	actggctcat	acaaaccaag	atgacatagc	tggaaactaga
18841	atcggaagt	gaggatgagt	tgtgttgact	Sattggctgt	cttcaagaca	tatacggttt
18901	tgggtcaaaca	tagccctggg	atagctgtaa	ataactagta	gaatagtgat	tgatctgtta
18961	tctattgtgt	atatttatag	tactaacact	gttgtagcag	atcaatgaac	agaattagat
19021	tgatgaaatt	gatgaacaaa	tttataattgc	atatattgta	tattagcata	aaactaaatt

FIGURE 2-F

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19081  aaatcatatt gattttgtta tggggagaac attggatata atgggtattga tgggtgatat
19141  taattaaatt aattttttatt ttattatttg atattgtaaa gggattcctg aagggttggg
19201  ttttaaattc taatttttaa atttatttta tttttttgtc tggccattac cactcagagg
19261  agttttttaa aattctgtaa tggtaaaaaa tttcttaact gtctgttagt tgaaatagct
19321  gttgcttggg gagattctga tatattgtat gtttgagaaa gggtatcttt ttttaacca
19381  aatgggaagt aggatttcaa ttttaaagat atattttttt caaacgtaag aaagggttat
19441  tgtagacttg aaattaactc tttctgccta agataatttc tccagtatat ttcttttttt
19501  cttttccttt ctctctcttt tttttttttt tttggaacat agcacagagt cattctttga
19561  tgactaggaa attttgtctt tgcagcctat ggaaaaata gccaaaggcc ttgatttttc
19621  tcattgtcat tattaccag ctaggtttgt aaataaatat gggttatctc cattctcca
19681  gtgcataatg acaaaaaaga aatagtact aattagatga agaagttatt tttcagatat
19741  cagagaaaga taagatttga tgtattgctg atccctatag aaagataaaa tttgatatat
19801  tgctgatccc tgtagtggga gtctgactaa tgtactatat ttggagaatg aggggttggg
19861  taagctatta ggagtgggtt ttgtggaaaa atgtccattc ttctaataat agttaacaaa
19921  cataaaacat taaaaatttt ttaaaaaatt gctttctatt caggcatggg tataaatcaa
19981  aaacagaatc aaggagtctc aatttacctc tcatttgaaa aaataattaa ttaattggca
20041  ttggcaacta ccaaaacaaa atcacaaaaa tctctgacat tttgtaaaat ttaccaagta
20101  atagcaaagt tggattgggtc tcaatttttg tcagctaccc acacttctgc cccagttaat
20161  ctactttttg cgtctatcgt gaagttttga ttgataaaaa gccttctaga aggttgatcc
20221  agaagaaaaa gaccttttct tactcttcca tctcctagct ctcttaatta tggcattgct
20281  tcccttctag agcctaaggt gtttcagttt tctttagtca gtgtgcataa aaaatctttc
20341  tgtgtcttag aagtgttgag tcaactctgg ttattattta ttaaatcata attttaaaat
20401  gtcaagagat tactattatt gttattttta ccagatgtga tttttcttgg taggttgggt
20461  ttaattgctg tgagtgggtt acaaaatcat aattttctta atgctttaga ctgataaaag
20521  aagtcacttg tttgtgagta atattgggtc cacactcttg aaatccaaga agcttaaaaa
20581  tccaagtgtt ttgtaagggt cacacaaact tacttgatgg caaagcctaa cggaactggg
20641  aggagtttat ttgtagtatt tatttctcat actctgtaaa taggatttat acttttctcc
20701  gcagaaataa tgtttgatta taggataata ccatggactt cactgggggt attagtgtaa
20761  tatatggtgc atgttccatg ttacccttga aaatctgaga aattatgaat tctgaaacac
20821  atctggttct taaagtttca gatagggaat tgcagaccg tatgatattg ctcttgtatc
20881  ctatgcaagg ttgttttaga taagagtgtt ttttccagaa cagtccaag taagctatgg
20941  atacctacat gacagtgtgt agattgataa tgatttcata gggtcagtca gtatctgtta
21001  aatgttagtg tttatttttt atgcaatttt gcttgcagga tgtttttgtt agcagctatt
21061  tgtatgtgac ttgtgggggt cactagatcc cagatactaa ttacagacag ctttctcaa
21121  ttttagtgct tagttaatta cagagggtta gcctagtgtg gttaatagaa attaaaatga
21181  tgtggaaaca ctttactttt tccaccattt tatcattacc ttttcttgg ctataggtgc
21241  aaaaaaattc atcatcctgt ggatttttact ggctaagact taactgggtt cttccccatc
21301  tcctactgct ccctgtcctc tttccctcct cccatttatt tctcgcttca aagattttag
21361  attgttattt acttaatttg gtacaaaagg aatgattact gagtacttac tgagtaatga
21421  ttactgagtt actaagtagt gttgggttga gagggactgg gctgccctag gcaggagtgg
21481  aagaaacctg ctagaaagct tacagtcctg tgagctcttt aatgtcttca gcctaacttt
21541  ttagtaacct ctgtgactgc tcattttcag gatggactgc tttattcatc aatttcttcc
21601  attctagacc atatagtagt tactgcgtag aagttttgaa agtgtagtga ctcttctttt
21661  attgatacga acagtatcct aataaacagg aagattgata atttctcttg caacttctct
21721  tttctgtgcc attgtgtgtg tcttttttca cctgtgttct tggttattcct aqaatttgtt
21781  tgggtatatta gagtgttagt ataagttgac tatcataaat atctatgctt attttactgg
21841  gtaaaagagta aaataaatga agcagtttta tgggttagat ttatcttgtt ttggttttga
21901  ctcaatactt acaagtcctat atagtttata aaagatgttt aaggaggaa gaattttgtc
21961  tgtattatca gtaaaattaa aatcaagtgc ccaatcttaa aagaagcaca ttacttttaa
22021  aaaataattg ctttttcagt accaaatatt gccatatgac acaaattagt gcttctcttt
22081  ttaaagcata ttttaattta gggttatcta tattcatctt cattagcact atactgaact
22141  aaaaccattg tatcaacttc attgatttat tatttgatca ggttgggaat gtctaccatt
22201  ctttgactta aatttgttta tattgttttg caagttattc acaaattttg gtggtttcat
22261  ttgtgtcagc gttgtgtgtg tgtgtgtgta tgtatataca tatgtgtggg ttttttttct
22321  tcatattttc aacagattct gaagggagtg gtaatggaag tgaagatgct tcaaaggaca
22381  gtggagaagg ttctgtagt gattctgaag aaaatatttt agaagaagaa ctgaatgaag
22441  atattaaagt aaaagaagaa caacttaaaa attctgcaga ggaagaagta ctatcatcag
22501  aaaaacaatt aattaaaatg gaaaagaagg aagaagaaga aaatggagaa agacctagaa
22561  agaaaaRgga gaaagagaag gaaaaaaggga gaaagagaag gaaagagaag gaaagagaga
22621  aggaaaaaga aaaaacacaa gtatctgaga atgtggctgc ttctgctgct gccaccacac
22681  cagccacaag tcctcctgct gttaacacat ccccttctgt tccactacg acaaccgcta
22741  cagaggaaca agtcagcgag ccaaaaaaat ggaaccttcg acgaaaccga ccacttctgg
22801  attttgtgtc catggaagag ctgaatgaca tggatgacta tgacagttag gatgacaatg
22861  attggcgacc tactgtagta aagagaaaag ggagatctgc gtctcagaaa gaggggaagt

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FIGURE 2-G

22921	atggagacaa	tgaggatgat	gaagatgagg	gaagcgggag	tgatgaagac	gagaatgatg
22981	aaggcaatga	tgaagatcat	agtagccctg	ccagtgaagg	gggttgcaag	aagaagaaga
23041	gtaaagttct	tagcagaaac	agtgtgatg	atgaggaact	gaccaatgat	agcctgaccc
23101	tatctcaaag	caagagtaat	gaggtagatc	aacccaattt	ttatatctgt	ctgtctgggg
23161	aaaagggaa	tcttctctaa	atcactctac	acattgtatt	aagtggcttc	cttgaatcc
23221	tatttataga	cggctgtggg	atgaatgagc	accctaactg	taacattttt	tcatttggcc
23281	aacagacttt	tattaaatat	ctactatttg	tcaccgttct	caaggagctc	acaatctctg
23341	tcctcaagga	gaaatattta	gagaaatatt	tttatatcca	tagacttggg	aatgacaaa
23401	gttttccatt	ctccttttta	tccctttact	cctttgttca	caggactgct	gaatgggtgt
23461	gagtgcatta	tgaataaata	ggtcaccttt	ccttcaactt	agttgtgtcc	atatccatat
23521	taaaatatag	gccttttaga	taccttagag	cagggcaaca	gtctaattgat	tttctgaaac
23581	cttttagagat	tcgtttttaa	tattaaattcc	tttaccagtt	gtagcactca	tcattctttt
23641	agtcaccaaa	tctttgtctt	atgtgtatgg	gacatacaca	taagtatgaa	ctattttttac
23701	atatattttag	taataaaatt	ctctctacaa	agaaaaggaa	taaaaaccca	aacattttcca
23761	tcataaaaaca	gacatttttg	tcacaaaact	gcagtaattg	ctcagtgtct	ctacttgaag
23821	ttctactact	gaaagttagg	tttattcatt	gatctcagag	atgcattcatt	caagactctt
23881	cagtcaaaca	catttgtgtc	tctttgtctg	tgtgtttttg	tatatgtttt	tcttcaaaaag
23941	aaagattgag	ttgttgtctt	acatgtagat	gtatctgtta	catcacatgt	agaactgtaa
24001	taattctgtg	atttctgtta	atgtgtttat	attcaccaaa	attttattct	ttaccaaaaca
24061	cttatttttt	tccatatcac	tgaagtaagt	taaacgggta	gaaagatttt	tcctcttatg
24121	ctttattttgt	tctttcacat	ttttctgcct	acaagtttta	catagcagtg	attatctatt
24181	ttaattgctt	tgcttaaaaa	tttgggtgatt	tcgttaccaa	aataatctat	agcaggctgt
24241	gaggttatca	gtggagatga	gacagcagtt	tatatttgga	ttataaacat	tggttaactt
24301	ctgaaaccaa	tattttatat	gaaaaaatat	tgccgtgcct	caatgtcatt	ataattctta
24361	cctttaaagg	aaagttgtca	tttgggaaat	agtgtaatat	ttttaatgat	atagcacagg
24421	cagttccata	ttatcaatgc	tatcttaaac	aggcatggaa	aaatctaatt	gtttgtattt
24481	aattgaggca	tgcatgcagt	ttacgttata	gcagttaata	ctctatatat	aatgaataag
24541	tttacttttg	accacatcac	tttcttcatt	tttatttaggt	tgatattctt	agaagtagtc
24601	tagctaatga	tagaggcagt	gtcgattaga	tttatgctaa	aatgtggggg	acacctgcac
24661	gtgttttagga	atttgccacg	taaagtgtgt	gtagtatctg	tttattaaac	ctgtacttca
24721	taaatactgc	ctaagagggt	gtagactaac	atttatgatg	catttaaagt	ccatgtgttg
24781	gttgttttagt	tttttttccc	cactagaaga	cacttttagta	aataaaggga	cctttttatg
24841	ttaggttaat	agtoccaaac	acaaacacat	tccaggaatg	agattccaaa	gtgcttcttc
24901	gaaaagtgcc	catgtagaag	agattataaa	aaggfacttt	ttctccagaa	taattctcct
24961	taaaagcttg	agtcattttt	ccctcaattc	tattattcaa	gctctacagt	agttttttga
25021	tgatttttagt	ttattttaat	tatgtccctc	aaattagata	attacatttt	aattaaaaaa
25081	ctaatacaatt	gtgattatta	gttatatttc	tagttttctt	atttgtatga	tcttaatttt
25141	gtgaaaagat	gattaaagct	agtccttggg	gcctgtggcc	aatgtttggg	tcttaattctt
25201	cctgggttatt	ttagctagtg	ataattttctg	tgtccaatac	atagtttaagt	atatatttga
25261	ttatatattga	agtttgattt	tccctgcttt	tactttgttt	tcagaaacta	cctttagtaga
25321	gagtttaggtg	aaaatgtagc	tttagaaata	cataatagaa	atatataatt	ataccatatt
25381	tagtttataa	gcaggcagac	atttttctta	gctgctaagt	tcattttgtag	caaaataatg
25441	accataaact	ttcataattt	tgaagtttct	taagggaact	tgatatttat	tttagcaggg
25501	ccctttttata	attactgctc	ttaatggcct	taacatatgc	ttaatggcct	taacaacatg
25561	ctgcagaccc	tgaaatactc	tctagcagtg	attctcaaac	tgtttttttt	tttttttttt
25621	tttttttttt	tttgagacaa	gggtctcact	ctgttgccct	ggctggagta	cagtggcatg
25681	atctcggctc	actgcaacct	ccgcctcatg	ggttcaagca	attcttctgc	ctcagctctc
25741	caagtagctg	ggactacagg	tgcatgccac	catgcccagc	acatttttgt	atttttagta
25801	gaggtggggt	ttcaccatgt	tggccaggct	gttctccaac	tcctgacctc	aagtgatcca
25861	cctgccttgg	cctcccaaag	tgctgggatt	acaggcatga	gccaccacac	ctggtctcat
25921	tttaaaattt	tttaaatgtt	tatttttttt	gagacagatt	ctcgttttgt	ttcctggact
25981	ggggtgcagt	ggtgtgatca	tggttaactg	cagctttgat	ctcccaggct	caggcaattc
26041	tcccacctca	gcctttggag	tagctgagac	tacaggtgta	cgacaacgac	tggctaattg
26101	ttttattttt	gatttttttt	ttttttttgt	agagatggta	tatcactatg	ttgcccagggt
26161	tggtgtcaaa	ttcttgacca	caagcagtc	tcctgcttct	gccttccaaa	gtgttgggat
26221	tacaggtgtg	agccaccaca	catagcccct	ttacagtttt	aaaaattatt	gaggacaacc
26281	attaatatatt	gtgtagatta	tatctgttga	tatttaccac	ttcaaattaa	aactgaggaa
26341	gcacacaagt	tatcagatcc	cattttcatgt	agtgtctgga	aaacttcatg	gtactcccat
26401	gagagaaaaga	gtgaaaaaga	gaaataatgt	cttagtatca	ttatgaaaac	tgccctttacc
26461	ttttatacct	actgaaagag	agttcactgg	accacacctt	gagaactgct	gctctagaac
26521	tgggcatttag	ataaactgca	ttttccgcaa	acggacacct	gtttttgtca	ataaccttat
26581	ggcatttttt	aaatttagtg	cagcctgaag	aatcccttgg	aaatgtgggt	gtatgtcttt
26641	ttcagccgtt	aatcttgag	cttttgagatt	ccttaagatt	atcttgccct	ttagttttct
26701	gaggtaaagt	ttttggggac	ggcagtgtag	tattttcaga	aatggttccc	attttcaaga

FIGURE 2-H

26761	ttttgaaact	aaagttttgc	atgagaatta	atccatgacc	gtaaaattata	tcaatagaat
26821	tggcattttt	gttttgtaaa	agaaagaaga	gctctgttct	cacagaaaat	atttaaaatt
26881	agagacagtt	tggatttttg	attactgctt	tataaatgta	actttatgtt	ctttgctgag
26941	tagaattttt	tttccataaa	agtctccgtt	aagtacatta	gatgtcatgt	tgagaaatgg
27001	caattgtcac	ctgatttttg	tgaattaaaa	tgtaaatgtt	ttgccaaaat	ttataaatat
27061	ccacttctat	ttgggacttc	taacttatta	atcagttgtc	tttttacaca	ttgcaaaatg
27121	aaacaaattg	ctctgagtcc	taaaaaaagg	tYagttctgt	aacattttata	aatatcgaga
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27241	ttataataat	tttttcttat	cttcagggca	gtaggattct	tttaattcta	attttacagg
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27421	tagagcctgt	ggagaaacatt	gatcagttat	atcatttttg	gggtaagttt	taaatcctga
27481	tggaaagaat	gcaataattt	actataagta	gtgattgatt	tattcatata	ctgtcattta
27541	ttcttctctat	aattacattg	gattccatta	aattattcca	tcataataaa	gttttttctt
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27661	atattttaga	aatttttatgt	taaaagcttc	agcttaacta	ctttctctga	aaccttgaaa
27721	gatgatatac	gtcttcagaa	atatactaac	aacagttgat	ataaatcag	gttttgattt
27781	gatctaatac	taagtgtgct	taaacttggt	tttgatctgt	taaaacagat	ctagctgggc
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28141	acatttctat	taagagcctc	aagtcagtag	gatcagaggg	ccagaaacat	tagttaatgt
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29221	gtattcaagt	gtcagttaca	aattgctgtt	gaaatgatgg	ctccaaatgt	tacttttgga
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29341	atataatatt	tgtattgtat	gaaactaatt	tatttaaattt	atttctgaat	attgttaggt
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30361	aatagcaaa	cagatcaaca	gtagttagtt	gcatgcgtgc	tttttcata	cctagaggag
30421	agagaatacg	aagcttgca	agaagtga	aattaaataa	gaggggtgct	acagggttct
30481	ttgataaaga	ggtcaagtat	atatttctca	aatataatgt	actttgaagt	taataaaga
30541	atggaaaaat	gggcatacat	ttggaaatgc	atataataat	gtttaagtaa	taaagaattt

FIGURE 2-I

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30721 attctgattt gctgtgtttg tctgggagat aatagtgagg acgctgatga aataattcag
30781 tgtgacaatt gtggcattac agtccatgaa ggtaatgttg ctttcttttc tctcttttta
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34321 tgaacccagg aggcagaggt tgcagtgagc tgaggtcgag ccactgcact ccagtctggg
34381 caacagagtg agactccgtc tcaaaaaaaaa agatcttgaa gtggtagcat gcttaagagt

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FIGURE 2-J

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38161 agggaaaaaa ggatatatgg gtccagatgt agctaggttg ttagatgtgg tagttggagc
38221 atgtgtaagt tatttttaaa atgtttcttg ttttctcagt gaaataggaa gcaagccat

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FIGURE 2-K

38281	tagcagagag	tgggacagt	gggagttaga	gatttgggga	ggcagagttg	tataaattta
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38401	gacacatata	tgtatatata	cacacacata	cacagcaata	agaccacttg	atattagtg
38461	taatgaatat	aaagagctca	ttaatatata	tatatccata	tgaatatgat	attagtggt
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38581	ggtgtggttc	agattccctg	gagtaggtaa	agaatatggt	aactcaggag	tagcagctac
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39661	agcctcggt	ctggaaaatc	taccttcttt	ccaaagtagc	tttgattttc	agaaacattt
39721	aaaaagtctg	aatcaaggca	gacaaatgag	atgatcaagc	tgagtggtaa	tgccaattaa
39781	gtcaacagga	tggtgtgtct	atataaagtc	atgtaacaac	tcttcttgtg	taattgattt
39841	aactgacttt	gatggcagtc	caagtataaa	atatttttga	gactttgcta	atgataactc
39901	atttaattcc	taaaactaat	tcattagaat	tggagacct	tttttggtac	agagaaggaa
39961	gaaagtagag	aaggagaggg	aaattgatgc	ataaataggg	aagctgaata	gtctttgacc
40021	actttagggt	aatctttatt	ttgtataatt	aatttattgg	tagtaatttg	aatctctgta
40081	actttatata	tgttccaagt	aaagatgcaa	aagatgcaaa	aagggtcaaaa	atacgttttg
40141	acttaaaaaa	ttacgtctact	actttcatcc	tctagtttaa	ataatttccc	atttcccttt
40201	ttaatTTTTg	agtttctggt	gtatgattga	ttttgtatgt	tgtattatta	gactttctgt
40261	tgatgatgt	ggagtatctt	ttcatatgct	tatttgcttt	tttttttttt	tttttttttt
40321	tgagatggag	tcttgctctg	ttgttctggc	tggagtgcag	tggtgggac	ttggctcact
40381	gcaacctctg	tctcccaggt	tctgtcgatt	ctcgtgcctc	agcttctgt	gtagctggga
40441	ttacaggcac	acaccactac	acctgactaa	ttttttattt	ttagtagaga	tgggggtttg
40501	ccatgttggc	caggctgggt	tcaaactcca	gacctcaagt	gatccacctg	ccttgggtctc
40561	ccaaagtgtc	gggattacag	gcgtgagcca	ccacaccac	ccftatttac	cttttggtata
40621	tcttcttgga	tgaggtgtct	attcagatct	tttgccatt	tttaaaaaatt	gggttggttt
40681	cttattgtta	agttttaaga	gttccttgta	tattttggat	atcagttctt	tatcagatag
40741	gtcttttgca	aatactttct	cccagctctg	agtttgctct	tttattctct	tgaagggtatc
40801	tctcacagag	cagaagtttt	acattttta	ggagtccaac	ttataaatta	tttctcttgt
40861	ttattacgtc	tttggctctg	tatcttaaaa	gtcgttacta	tgctgaggt	tatctagatt
40921	ttctcccgtg	ttattttcta	gttctataat	tttttaatta	taaaatttct	taattaaaaa
40981	tttaaaaaatt	tttataaatt	tgcatttcac	atttgggtct	gaatttattt	ttgttacgag
41041	tatacgggtc	gtctcggaa	tcattatttt	gcattgtgtg	gttcaatttt	tctatcacca
41101	tttggttaaaa	aagctgtctg	tgctccctta	tattgccttt	gtcctttgt	caaagatcag
41161	ttgactatat	ttctttgggt	ctttttctgg	gtcagtttg	ttcatcaact	gacctatata
41221	tctattcttt	gattaatacc	acactgtctt	gattactgca	gttcatagt	aagtcttgaa
41281	gttgagtgt	gttactcctt	tgacttggtt	tttttcttct	aatattatgt	tagctcttct
41341	gggttttttg	cctctccatg	taaactttag	agtcagtttg	cagtatctac	aaaattacat
41401	cctggaattt	tgattgggat	tttattgaa	ctatagatca	agttgggaag	aaatgacatc
41461	ttgacaatat	tgagcttttt	tattcatgaa	cataataaac	atttatttat	ttagttcttt
41521	gatttcttct	atcagagttt	tgcagttttc	ttcatagaga	tcttggcaat	attattttat
41581	tttttggggg	gtgctaattg	aaatggaa	ttgtttttta	tttcaattct	acttggtcat
41641	tgctttcata	agaaagcaat	tggcttttgt	atattaagtt	tgtatgctgc	agtcttgcta
41701	taattgcttt	ttagttccag	gaaatttttg	gctactcttc	cagattttct	acttagacag
41761	tcagtgcac	tgaaagcaaa	gataatttta	tttctttctt	tccagtgtgt	atatttttgt
41821	ttccctttct	tgctttatta	cctgattgtg	aaagcagtac	tgacagagaa	catccttgcc
41881	tcatacctca	tctttgtggg	caagcttcta	gtttctcatc	gttaagtatg	atgttagcta
41941	taggtttttt	ttgtagtctt	tttatgtctt	agttgaggaa	attactcctt	atttctgttt
42001	gtgttttttt	tttacttggt	tgttttgaga	cagagtctca	ctctgctgcc	caggctggag
42061	tgagtgggc	caatttcggc	tcactgcaac	ctctacctcc	tgagttcaag	tgattctctt

FIGURE 2-L

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42121 gcctcagcct cccctaattgt gtataatttt aaaaggtgcc tcaagattcc tcatgcagga
42181 gatgggaagg atcatccttt gagagacatt ggtttagaag aaagtaaaaa tggggggata
42241 aaaggaactc tgcaatgtgg acgatgtcat gctggagcct agacagccac aggtgtaggt
42301 caagggggga gccagagcaa tgtagaatga agtatggttc ctggtataag gcaaataatca
42361 gggtgacagt gaggtttcta aaaattaaga ctttttattt tattttattt ttattttttg
42421 agacggagtt ttgctcttgt tgtccaggct ggagtgcaat ggagcaatct cgactcactg
42481 caacctccac ctctggggtt caagcaattc tcctgtctca gcctcccaga gtagctggga
42541 ctacaggcat atgcgccacc acgccagcct aattttttgt atttttatta gagacgggat
42601 ttctccatgt tggtcaggct ggtcttgaac tccccgcct ctggtgatcc actcgcctct
42661 gcctcccaaa gtgctgggat tacagactg agccaccgcg cccggccaaa aattaagact
42721 tcttaatcct cttaataatg gttagggcaa acacaggaaa gaagaggcaa aaatgaaatg
42781 ctgatgacaa aaattaacgg tgtgagcacc aatagaagg tgggggtcaa tgcagatgga
42841 agcttgggta gtatctgcta aagagatgtg ccacctcttg ctccagctct tctactgtct
42901 tcagggtgat ttttctttct tttttttttg agacggagtc tcgctctgtc accaggtgg
42961 agtgcaatgg catgatctcc gctcactgtc gcctcccagc ttcaaggaa tctcctgcct
43021 cagcctccca agtagctggg attacaggcg tgtgccacca caccagcta atttctgtat
43081 ttttagtaga gatggggtt caccatgttg gccaggatgg tcttgatctc ctgacctcgt
43141 ggtccgcccg ccttgccctc ccaaagtgc tggtcatac tgttcatatt atttctgtct
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43261 cctgaccatt tgaatgactt gtctttttct ccagtgtttg ggggctttca tatatgcttt
43321 tccttttacc cagattcctc ttgttccaca aatataacct aaatacatag gtgttaagcc
43381 agtgtttacc gtttgtcttc ctgttatttg gagatttgaa aaatcttact ttaattttta
43441 tttttaaata ttttattgtg tatatttcag gtatacaata tgttgttatg ggatacatat
43501 agatagtaaa aaggttactg tagtgaagga aatgaacata tccatcatct cacataatta
43561 cccaattttt aaaaagttaa ccaagtccat cctctgcag aaattaccta tttttttgtt
43621 tttgtgacaa gaacagctaa aatttacatt taacatgaat cccatacaca gtacaagttt
43681 attaccttga attaatcat taaaatattc ttaattataa gtgacatatg agtagatatg
43741 taaaaatagt tatgctgtct gtctcaactc tacttctctt tgcataaggga atcactgtta
43801 acaatttggg atgtatctac ccatctgtt gtacattgtg taccagggtt ttttaactt
43861 tattttatta tgtagatata tgtcctctgt ggaaacatc agtagaaata agctaagaaa
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44041 gtctctacaa aatacagaaa aatcagccag gtgtggtggc ttgcgcctgt agtcccaact
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44521 ctgccatttt gtgggtgttca tgatgttgac atattgaaga atcttagttt ttataatgtc
44581 atattgaata tctctcagtc tggatatatc tgattgtttt cttgtgatta gattcagttt
44641 aaattttttt ttttttttgt aagagtattg tgctggtgtt tagttcccat tatatcacat
44701 caaaagacgt ataattgtgc tgggtgcggt ggtcactgcc tgtaatccca gcaactttggg
44761 aggccgaggt ggggtggatta cttgaagtca ggagttcgag accagcttgg tcaacatggt
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44941 actgcactcc agcctgggca atagagcgag attccgtctc aaaaaaaaaa tgtataatgt
45001 caatttattg cattattggg gatagtttag gtgatgtcaa ccacagacct ctaattttta
45061 aagggttttt ttttctattt gtaattaatg ataaatctgt ggggtaataa ctttgagact
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45661 agtttttcac ttatatatag tgctgacaaa catgtgccat gtatatatat gtaataatth
45721 ctgtgggata gatacctaga agtaaaaatt cttttttttt tttttttttt tttttgagac
45781 ggagctctcg tctttacca ggctacagtg caaaggtgag atctoggctc actgcaacct
45841 ctgcctcctg ggttcaagcg attctccgc ctcagcctcc tgagtagctg ggactacagg
45901 catgocccac ctccccgcg tatatttttg tattttgagt agagacgggg tttcaccatg

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FIGURE 2-M

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45961 ttggccaggt tgggtctcgat ctccagacct catgatctgc ccacctcggc ctcccaaagt
46021 gctgggatta caggggaagta aaattttctta gtcaaaagat aagtgtattt aaacttctaa
46081 aaaccatttc cagattgact accaaaagga ctgtactaat taccaacaat gcacaaacta
46141 cttgataaca ttgcatattt gttaaattttc ttttattctt ttggatataa tctctttatt
46201 acaatgtgca ttacacttat taagaatgaa gtttggcatc ttgtggccat ttgccacatt
46261 ttgttttctg ttacttgcct gtcattttct tagtcatttc ttttcttttt ttttctgggtg
46321 aaaacataca catatattta gaattagcca gctggactca gtttagatga toccaatttt
46381 gttggcaaga ttcaaagcat tgtaatcagg agccagtcga acatatgcct tcttttctcc
46441 atcaggccga attaggggtg tgacaccttg gccacatcaa tgtcacagag ctccctcaca
46501 gctgttttga tctgggtgctt gttggcttta acttcctcag tgaacacaag catgttggtg
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47581 taaatatgaa cttcatgaat actttattta gagaaaacta tttgcctatc ataatacatg
47641 aatattaaat aaaatgtgga aaatatagaa cagagagaag aaaaaaacat ttctaattgt
47701 cctcatatoc agacagccat agtattttgt tgcatctctt ttatctcctt ttttttgaga
47761 aatatgctta ttctcaagta attgcataag gatctttaag ttgagatttt gctaaaagat
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49381 aagattgatg ctaattaaat ggccatagaa acatgtcttc tgtgttacct attggaacaa
49441 cactgagcac atatgagttt tatgtgttta tacattgttt attttgttta cccatatgaa
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49561 atttagtcac taattaaaat gaattggagc agatatacag tgctagaact ttggtctaga
49621 gctcagtaaa cccaacagg atgacagaga aatatgggat aagtggcagg taaaagtggc
49681 aagtaaagaa ctctataaag gtaatgacac agtatggatc atttttcagg gacagtgaag
49741 ctgaagaaaa aatacatata gacttgctgg ttgttctttg agcttgcaac acaccattct

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FIGURE 2-N

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49801   tccagattac aaaggaagaa tttcctggga atggatttca gaatcattcc taagattaaY
49861   tgtaggaggt ttaaaactct gtgcaaatgt gcacgtttgc tatgtgtgtg gaatattctt
49921   taaaaatata attgaaaatt ttctttatct tgaaaaagt aactgctgtg atttaccttg
49981   atttggtctga atgaagttaa taaattggat agctccttaa gggctttatt ctcttggtaa
50041   ttgctacttt gtgtggatgc acattttatc tagtttgaat ttgtttcaaa ggaacattat
50101   tttgtaaaata aaatatatat tttttcccat gtggtattgc atagcacatg gagaaaatag
50161   attgatgata ccgtttcatt ttatgatttt tctttgaata taatgttttg ttcttttatt
50221   ggaaataaaa ctgaccccaa gaataaaatt atatttcctt ttaattttat gatagtgcac
50281   ttaaagtaaat gtatatctac ccaaggtgat gaagatgatg attgcccaacc acaattttaat
50341   gacattaaag aaattaatga gttttgatct ctttgcttat ctgtgtgtgt atagtctaac
50401   tcctttttaa tctgttcttt gacattttat atgactttca gattgtgtgc gtatatatga
50461   tacatataat tatgtattaa agtatgttaa ttaaaaatgt taattaaatg aaattaatta
50521   tatagtttaa tttgtacta ttaattattaa ctatatttag cataactatt aacatagtat
50581   atatgaaatc catatataca tatatatata cacacacaca tgcataatct gaaaaaatat
50641   atatactttt ttgagacgag attttgcctt gttgcccagg gtggttcact ggcacctcc
50701   acatcccagg ctcaagtgat tctcccacct cagcctttct agcacctgag actaccgtgt
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50881   agcattggga ttgcaggcat gaactacacg ccttggctga ctttcagatt ttattaaaat
50941   tcaactgttat aaaacctttg aatagcataa ggataacaat taaacagttg ctgacagcag
51001   cttgtgtaag tcatagctgc aaaccaactt tttagttttt tgcttactat taggctattt
51061   tagttatgat ctatatttgg taagtagtgt tttaatgaaa tacttacatg taaccactga
51121   catataatga cgtctagtta attaatgttg gtaattttaa attatttact aattgtatat
51181   ggctcttttc ctttctcgtg ggtgatttgt ttaactcagt attcattcat ttatatactg
51241   tagttattta ttttagtttg aatttctttg atggttgtga gaggtcacgc tcaaatctag
51301   gctcctgggt gtctggttag tgtttaccag ttcaaataat cacatgatct tacattggat
51361   atataataac ttaccatata ggtgaagtct tttaggagac gatcatgtta aatgtttctc
51421   actgtggctt atttaatgtc atcagtttat tgcgtgttac tttggatgcc ccttagaact
51481   tggcaccaag acctacctc ttagaataaa cctggtcaaa aggatgttgg gatggttgc
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51601   aaatgcccaa acctaaaggt gatacttcag gacaagaatt aagttgcaat gtgttcatta
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52621   ggtgtgttca tgagaatctt taaggatttt tattacatta gctgcctaaa taatatgatg
52681   aactcctctc agaattgttg gttttgtgag tgataagagg aaaaaagaga atgacatatt
52741   gttttcatcc atttcagtta tagacaaaatt ttcacagaaa gaataattta aatttttga
52801   acagattaaa tacatcatag agttagagat tggctcagtt gtgcatggaa ctgagctgt
52861   ctaatgttac tactctgaac ttttcaaact gttctatagc tttaggtgca taactttgct
52921   tttacaattg tattatacct gtttgtatta taatctgcca cctccaaaat tagatcaaag
52981   actttttggg ttgtatcttt gttttgatg agtttgatct tttatatata ttttttagta
53041   cctgctacaa agggacctca Rtaagtgttt gccaaacca aattaatcta aattctttta
53101   tgacaacttg tattttttat atttttatat tttatttttt atgagatgga attttgcct
53161   tggcacccag gctggagtgc agtggcgcaa tcttggctca ctgcaacctt tgcctccagg
53221   gttcaagtga ttctcctgcc tcggcttctc gagtagctgg gattctgggc gcctgccacc
53281   acgcctggat aattttttgt tttttaggag agatgaggtt tcaccgtgtt ggccaggctg
53341   gtctcgaaact cctcacctca ggtgatctgc ccacctcggc ctcccaaagt ctggggaata
53401   caggcatgag ccaactgcacc cagcctaatt tttatatatt ttaaaattaa aattttattgt
53461   tttcccacct ttaatgcttt tacagtagga ctaaaactat ttttaaaatg tcattttatt
53521   cattgtgtat actacattag gtgaaaaagt atataaaatg agttttattc tgtattttta
53581   tacgtttctt ataaaccatt ggtgtttcat atctttttcc tcatctcttt gctattcttt

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FIGURE 2-O

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53641  ttctttttgtg attttatgtg actttaacaa aataaacccct atttaaatcat agtgttttttg
53701  ttttttttag gttgttatgg agttgatgga gagagtgact ctattatgag ttcagcttct
53761  gaaaactcca ctgaaccttg gttttgtgat gcctgtaaat gtggtgtttc tcctagctgt
53821  gaactgtgtc ctaatcagga tggaaatttc aaggagacag atgctggaag gttaatgtcc
53881  taattatggt ggttcatatg tttgctttat aatgtgtctg cctttgactt cctgttctt
53941  ctgtttatga ttacacactt tcatttgatt gcttctttgt atcttcttgg catagaataa
54001  atgaccagtg ggatacagat ggagaagggg gagaggaaag accattttatt gactacctgc
54061  atttgccctt acatccataa tcttaattaa tcttaataat tgaccctatg atgaggcagg
54121  tggtaacggt tctcatttta taggtgtata gtaccagggt ctcagattat ttaaataact
54181  tattcggttc agaccacaaa aatgatcttc gtcaattttg aacctagatc tgtataactt
54241  tatatcagga gatagaactt aatcaggatg tttaaaaaga agtttagtat aaagaatttt
54301  taagctgtga taaaagagtc actataaggt ataaaaaac tctaaaggat gctctgggcc
54361  tgagggagat tatccaagga atgacaaaat tggaaatgat acctcctacc ctagggtggg
54421  gttcaggctt tgttgagaaa attatagtta aaccctactg gatggagaga aggccctctg
54481  tgttgagagg gccatggaaa aatgatcttc atgttgggcc agggctgtga ggtcactgag
54541  ggactgtgta tatagctggg gcagagcaca ggaggaagta ctccacccat acctgctgaa
54601  aagccctccc gttctacgag acctcctgcc attgagttta tagctccctc taccattgag
54661  cttagtgtta tgctcactct gagaagaaat gctgaagaaa ttctgtccat tattgcagag
54721  taggtattga agcatgcgtg agaggcaatt aataagtggc acaaagacct gtgttctttt
54781  tactacattc acactcatgt ttgttaacac atttgagcac ttgtcatcat aacggtgttg
54841  ccatcttcca tgtttttttt ttttttacag gagactacca tctagggttg gtgactaaaa
54901  ttaagagtaa ttttcaacct tttgtatttc gtggagatca cgctctgcct ctctctctcc
54961  aatataagag ggggggtggg tacttaaaat tttattttgt cacataagga tgttttagta
55021  ttttattaaa catgctttat attaaaaaca agattaacag caaagcaacc tatataaatt
55081  atcaccatca tttcccatat tttaacataa aaactagggt atattatgtc ctaaaaataa
55141  ggataggctt ttaaatttaa taaattttac tttagtaaag taaaacaaat tttctcttat
55201  ttttatcatt tttgcctcaa ttggtggact gatccttgag aaatgttgcc atacaagatt
55261  gctgggatag cgtagaatct accattgaat cttggagaat cccatgtgtt gatgttcagg
55321  acaaatgact aaagaatctt acctcttctt ccttattgtc tatccaaaaa taaaataat
55381  aacaaatgat ttgatgtatt gacatgaatc tgtggtctgt atcataggca taggcattac
55441  tctaagttgg gcctgagagt ggcctagtat tagggagttt agtaagcatt aagtgtgcac
55501  cttcaagttg gactgtctat gtttgatttc tagtcttttt tttttaatag ctataatttt
55561  aggcaagtga tgaacctttt ttatgcctca gtttccctag cagtgttgag aagactaaat
55621  gagatgatcc atgagaaaca actagcagtt tctgtaacat aataagtggg cagttaaatt
55681  ctccctactc ttactactgc ctgtactgct gctactagtg ctttcttatt accattattg
55741  ctccacttat tttaggtaat catggagtat tagctcatgc atagattttt tttttttttt
55801  tttgtaact cttccagtc tgaagaattga aattttttgt gataaattgt ggtgaataag
55861  taaggcagtt ttggaaagac agaacttcct tttagggaa agaatttatt ttactgtttt
55921  tcttgttgat aatttaaaag ttctgttagg acactgtcaa gtagtgggta tttcatgcta
55981  tcataataga caaaacaact ggcaaaagtt tttctgaatg aagaaaactg aggcctcttt
56041  accatttagg tttactgagg gatttttttt tggatactgt ggacgttaca taagtagaca
56101  cctcctgtga tgggtcaatc tggcaaaaat tcttttatat actatttgaa cactgtgtgt
56161  aatgtctaca cttacctgta ggctgtactg gaaattatag gccttcacaa tatttccaag
56221  gacgtaatac tagtttgatt aaaggttataa aaagccaaga aaattcgaga agccttttag
56281  tatatgagct tcaaattgaa aacagggaaa aagaaagaat attgtatata aagaataaaa
56341  aaggttttga agttcaccat cacatgagat taattagact tttttccttc tattcttgat
56401  gggagccaca agttctacat agaaaatgat gtgatttaat gtaagaaaac cagtacattc
56461  ttgtcattaa atttttattt tatatcttat ggagagtaag acttataaac ctgactgtgg
56521  gaaatttttt ggcattgctc ctttttttat tttttattta tagttttact atttggggg
56581  acatagtaga tatgtatatt catggggtac atgagatggt ttgatacagg catgcaatgt
56641  gaaataagca catcatggag aatggggtat ccatttctca aacactgtgc ttttgagtta
56701  caaacaatcc agttaccctc ttttaagttat ttttaagtgt acaatttagt ttttcttgac
56761  tgtagtcccc ctggtgtgct attaaacagt aggtcttagt ctttccactt tttcgactca
56821  ttaaccatct cccacctccc cccacctttc caccctttcc ctgcactatc cttcccaacg
56881  tctagtaacc atccttctcc tgtctgtgtc catgagttca gttgtttggg ttttagatcc
56941  cacaataaag tgagaacatg tgatgtttgt cttgctgtgc ctggcttatt tcacctaaac
57001  taatgatctc tagttccacc caagttgttg caaatgactg gctctcatto ttttttatgg
57061  cttagtactc cattgtgtat tgtgtaccac aatttcttta tcggattcgt ctgttggtgg
57121  aaacttaggt tgcttccaaa tcttagtact tgtaaacagt gctgcgacaa atataggagt
57181  gcagatatct ctttaatgta ctgatttcc ttccttcgga tgtataccca acagtgcagt
57241  tgctggatta tatggcagct caatttttag gaacctccaa agttttcttc atcatggttg
57301  tactaatWta catttcatgc aacagtgtac aaggggtccc ttttctccac attcttgcca
57361  acatttgtta ttgcctgtct tttggatata agctatttta actgggggtga gatgatattt
57421  catgatagtt ttgatttgca tttctctgat gatcaaggat tttgagtccc ttttcatatg

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FIGURE 2-P

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57481 cctgttttag catatgagct tctttttata tgtctttttt tgagaaatgt ctattcaaat
57541 cttttgtctg tttttaatca gattattaga ttttttcctg tggagttatt tgaactcctt
57601 gtatatcttg gttatattatc ccttgtagt tgggtaattt gcaaatattt tctccattc
57661 tgtgggttgt ctcttcagtt tgatgatgta ttctttgccc agcttggtgt gatccctgctt
57721 tttaaaaaaa cctgatatga tatctttcgt ctgtttttgc ttcggttgct tgtgcttggtg
57781 gagtttcgct caagaaattt taccagagc aatgtcctgg attccccaat gttttcttgt
57841 agtattttca tagtttgagg tcttagattt aagtctttaa tccattttga tttgattttt
57901 gtatatggca agagatggcg tctagtttcc ttctctgca tatggatag cagtttttcc
57961 agcaccattt gttgaagaaa ctgtcttttc ccataatata gttcctggca cctttgttag
58021 gcactaagtt cacttaggtg cgtggatttg tttctgagtt ctgtattttg ttcccttggtt
58081 ctgtgtattt gttttatgac agtaccatgc tgttttggct actgtagggt tgtggtataa
58141 tttgaagtca ggtagtatga ttcttttttg cttaggatag ctttggctct tctgggtcctt
58201 tttgtgttcc gtatacattt taggattatt ttttctattt ctgtgaagaa tgtcattggt
58261 attttgatag ggattgcatt gaatctgtag attgctttgg gtagtatggg cttttaaca
58321 atattgatcc ttccagtttg tgaacatgga atatttttcc attttttggt gtcgtcttca
58381 atttctttca tcagtgtttt atagttgtta ttatagaaat cttttacttc tttaaagttaa
58441 ttcttaggta tttaatctta tgtgtggcta ttgtaaatgc cttactttt aaaatttctt
58501 tttcagatta ttactgttg tcactgttag atgctcctga tttttgtatg ttgcttttgt
58561 cttttgcaac tttactgaat ttatcggttc taatagtttt cttatgaggt ctttaggtttt
58621 ttccaaatac aacattatat tacctgctaa caagaataat ttgacttctt tctttccaat
58681 ttggatgccc tttttatctt tctgttgtct gattgcogga agctagggtc tccagtacta
58741 tgttgaataa cagtgggtgac agtgggctg cttgtcgtgt tccagatctt agaggaaaag
58801 cttacagttt ttccatttca gtaagatggt agctgtgggt ctgtcatata tcgctttat
58861 tatgttgagg tatgtctttc tatcccgttt ttggggagtt tttatgatga agggatgttg
58921 aattttatta aatgcttttt cagcatcagt tgaaatgac atattggttt tatccttcat
58981 cctgttgatg tgatatatca tgttgattga ctgtcttatg ttgaaccatg cttgcaacc
59041 agggataaat cctacttggt cataatgac ttcttaacgt attgttaaat tgggtttgct
59101 ggtattttgt tttcttcatg tgcgctcagt ttcatcagag atactggct atagaatgag
59161 ttttttgatg tgcccttgcc tgggtttggt atcagagtaa cactggcctc atagattag
59221 tttggaaata ttccctcttc ctctgttttt tggaaatagt tgagtaagat tggattag
59281 tcttctttta gtgtttggtt aaattcagca gcgaagccat caggtcaagc agtccaggc
59341 ttttctttac cgggagactt tattattggt tcaatctcgt tacttgttat tggctgtac
59401 aggtttttga tttcttcatg gttcaactct tttaggttgt atgtgtctag gatttcaac
59461 atttctttta gattttctaa tttattggca tatagttgct catagtagct gctaagatc
59521 ctttgaattt ctgcaatatc agttataatg tctccttttt tatttcta atttttact
59581 tgtatcttct ctcttttttc ctcagcctgg cttaaagggt gtcagtgttg tttacctttt
59641 caaaatacta acattttggt tcattgatct tttgtatatg ttttttattt caattttatt
59701 ttttctgct ctgactttta ttactctact aatttttggg ttggtttgct cttgctttcc
59761 tagttcttta agatatgtca ttggattggt tttttgaagt tttttctctt ttgatgtagg
59821 tacctatagc tataaacctc cctcttagta gggcttttgc tgtatcccat agattttggt
59881 atgttgtgtt tccattacta ttctgaaatg ttctgtcctc tatgtccttt gttgggtgtc
59941 ctcccagctg tctgaaatg ggcagcattg ttgaactaaa ttccttaatt tttaaaaata
60001 agctttatgt ttgcaatagaa ctggtctctg tccctctctt gctcagttc tttctttttt
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60121 tggctcactg taacctctgc ctccctgggt cagggtgacc tccactgaa gcttctgag
60181 tagtgcaggt tatagggtgt cgccaccaca ccaggctggt gtttgattt tctgtagag
60241 acgaggtttc aacctgttgc ccaggctggt tgggctcaag cagtcctccc
60301 acctcagcct tccaaactgt taggattact gtaacctggc ttttttctgg
60361 agagaacgtc ttgctttgtc accctgactg gactgcagtg gcatgatctt ggctcattgt
60421 aaacccccgc ctctaggtc caagcagtc tcttacctca gctcccaag tagctgggac
60481 cacaggggca ttgccagaca cctggctaaa ttttgattt tttgtagcga tggggtttca
60541 tcatgttgc caggctggtc tcaaactcct gagcttaagt gatcctccta cctctgcctc
60601 ccaaagtgtc gggattacag gcatgagcca ctgtgctga ccacttcttt cttttttttt
60661 ctttaaaatt ctagatttag taagtcttag ttctgtccct tgctagactt gttatatattg
60721 aaaatcagtt aatttttctg aaaccaattc ttcatatgta aatgaacaac ctctactca
60781 acagaagctt ttaggctttt ttttcttgt agttaacatt tcttgagtga agacagttag
60841 ccacactctg ctgtaagcac ttacatatca tctttataac ttccaaacta ctttatggt
60901 gctctgtgcc tagtagacac ttataattga ttactgaatg aaggaatgaa aataacgtac
60961 ttgacgtgaa tttgttttac atgctgtaaa ggcattactg atacagagca cttcaaactc
61021 caattttatt gattaatata gttttcattc tttaatgagt cttttgagaa gtatcactct
61081 acttagtctg ctttattaaa atatatgaat ttacaataat ctgttaatat tttgtgctag
61141 ccagtacaat ctgactgttt tttggtggtt ttatgtgatg ctattttcct gttcctttcc
61201 cagatcagca tctgtcataa tagctccaag ggtaagtaa caaggaagat
61261 ttttttttaa attgtagatt tgtcttaatt acaagttat aaataatgtg catctaaaca

```


FIGURE 2-Q

61321	gatgagcaag	aaactatttta	cagctgggtat	taaaagggac	catagtgtgtc	tcggccatga
61381	ttttcattga	ctttgatagg	tatttttaatg	aggactcaag	ttggtatcct	cacatgagtg
61441	gttgggagaa	tgatatactt	gtatgccagt	cacattgaaa	tggcagttta	aatctgtagt
61501	acttgtgtac	tacatttttaa	gaagggtcagt	atgaagcaag	cagccagctg	ttaggtttat
61561	caRagataaa	ctcctacaga	gtatagcgac	atttaataca	tcagtggagc	atgaaaaaac
61621	tgaacaaatt	aaattgagaa	agcagctgct	tgttgaagaY	gtgtatcttt	atatgaaact
61681	ccataggatg	tatttgggag	gttggattaa	aacatttctat	caagaaaatc	tcaaaacctt
61741	ggcttttttc	cccaataaaa	aagataattt	tttaaaaaga	tttagaacta	tttttcccag
61801	tgctcttaga	gaataatttt	tggtcttagt	cctctaaaac	tcataatgca	ccacaaaaac
61861	cagaacctag	tagcatgcat	agcctctgaa	gttgtgataa	agcagaattt	gttgtaata
61921	tattcacagg	gttaatagag	atttgctgct	gtgacctct	ttcttacaaa	agtgctaaga
61981	tctactgttt	aaattttcaaa	gtcagtgatg	ccacattttg	ttttgttgta	agcaagcaga
62041	aagagtgcct	aatatatttaa	aaaagggttca	gagcagtttt	taaaaaatga	aattagaaac
62101	aactgcaatt	tttttccagt	tactgaaact	ctgagcattc	tttgttttag	tcttatagca
62161	tcattcaaac	tttaataaat	atttataattt	ggggcatata	aatttttagta	tRtagattgt
62221	atggtaaaca	gataagatga	ataaaaatgt	gaattgctta	ttctgtacct	tttcccagca
62281	gttttaatct	ggaaaggaag	ttaaaactgt	atacaaaaat	tgtaaaatat	gtccttaaag
62341	attattaccc	cagcagcttt	tggaaaagag	taataagaga	aattttacct	aattactgca
62401	gagtaaattc	acagttatta	aattagtagt	cttaattctc	aaagggtttg	aaataatgaa
62461	cggtgactac	tttccttgca	tatgaaaatg	atgttttggt	tcattttgaat	agtgatttta
62521	tgcaaatatt	taagaataga	taagtgcata	gtgcagtgg	tgaattttta	gtgaaaggca
62581	attatagttg	ttagctctca	gttttggtta	agctgctgga	aaagtaattt	cagtcccctt
62641	ttttgttaact	aagtgttatt	ctgtagggtg	ttcatatttt	ttaatgatgt	gcctgagatt
62701	gcgagatttt	aacattttgat	tacagaattc	tcttggtagt	attttgagat	ggcaagcgtt
62761	ttatatgttt	gttttggtg	tgggaatttt	attaaaagat	ttgatagcaa	aatcatatct
62821	tctcttctta	gatgggttca	tattgtttgt	gccctgtatg	ttcctggagt	agcctttgga
62881	gatattgaca	aattacgacc	agtaacacta	acggaaatga	actattccaa	atatggtgcc
62941	aaggtgagac	acaaagcatt	tttgattgct	tgaagagaaa	aggttttact	tgtagtttta
63001	cctggccttt	tatttgtatt	atgttgactg	cagaaatgct	tactaggaat	cattctattt
63061	agcactaaat	catttattat	tgatgtagtg	tttcctagaa	agccaataat	gcataaaattc
63121	ttctatacat	tcttaattta	gagtaacgta	tgaggtaaaa	tgataattgg	tactactacc
63181	atttccttgg	cagtggtcac	aatgccta	acatagacca	aaaccttatt	tacaattaga
63241	tggatcaaat	ataagcctaa	tttctgactt	tacttttgaa	gtggaatttg	tcaaaattat
63301	gaaaaagaat	attagaagtg	atcttttagt	ctgttactgt	aattgttttg	ggcggtgccg
63361	ttaacatgcc	cttaatagat	ggtgaactta	attgatatat	gttatgtgtg	ttctgactgc
63421	ttcaccaacc	tgggtgtccc	ctatctttct	ccctgacttg	gttggggcct	ctctgttcgc
63481	tgagacacag	tgaatttgaa	atttggccaa	ttagggctgg	gtgctcacgc	ctgttatccc
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63781	gactccatct	caaaaaaaaa	gaaaaagaaa	tttgccaat	taataattct	acagtggcct
63841	ctaagtgttc	aagtgaagg	aagagtcata	catctgtcac	tttaaattaa	aagctagaaa
63901	tgattaagct	tagtgaggaa	ggcatgtcga	aagcctaggt	aggccaaaag	ctgggcctct
63961	tctgccgaat	agccagtatg	tcagtgcaaa	ggaaaagctc	ttgaaggaaa	ttgaaagtgc
64021	tactccagca	aacacatgaa	tgataagaaa	gtgaagctgc	cttattgctg	ataatggaga
64081	aaattttaat	agtagggata	gatcatagca	gccacaacat	tcccttaagc	caaaacctca
64141	tccagagcat	gaccctaact	gttcaatatt	gtgaaggctg	agagagggtga	ggaagctgca
64201	gaagaaaagg	tgaaggtag	cgaggtttg	ttcatgaggt	tttaaggaaa	aagccatctc
64261	cgtaatatata	aagatgaaga	agatgcagca	ggtactgatg	gagaagcatt	agcaagttat
64321	tcagaagatt	tagctaagac	aaatgatgaa	gatttgtaca	ttcaacaaag	attttcaatg
64381	tagatgaaac	agtcttctat	tggagaagaa	tgccatctag	gacttaccat	agctagagag
64441	gagaagtac	tatctggctt	ctaagggcag	gctgtctctc	ttgttttagag	gtgaatgcgg
64501	ctggtgactt	taagttgaag	ccagtgcttc	tatactattg	tgaaaatcct	agagccctta
64561	agaatttatgt	taaatctact	ctgcctgtgc	tctgtaaatg	gaacaacaaa	gcctgtgcac
64621	agcacatctg	tgtaccgcat	ggtttactgg	atatttttaag	ccccttggtg	agacttactg
64681	ctcagaaaaa	agatttcctt	caaaagatta	ctgcttatcg	acagtgcacc	tgggtggtcac
64741	ccaagagctc	tgatgaagta	caaggagatt	aatgtgtttt	cctgcctgct	gtcacaacag
64801	ccattctgaa	gcccattggat	caaggagatca	ttttgacttt	aaagtctgat	tatttaagaa
64861	atacatattca	taaggctata	gctgccatcac	atagtatttc	ctctgatgga	tctgggcaaa
64921	gtaaattgaa	aaccttctag	aaaggggtca	cttttttaga	tgctattaag	aatatttatg
64981	attcatggga	ggaggtcaaa	atatccatat	taacaggagt	ttggaagaag	ttgattgcag
65041	ccttcatgga	taactttgaa	ggggttgaa	aattcagtg	aggaagtcac	tgcatagtg
65101	gcagaaataa	caagataact	agaattagaa	gtgtagccaa	aggtgactga	actgctgcga

FIGURE 2-R

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65161 tctcatgata aaaatTTGaa cagatgagaa gttacttctc atggatgagt gaagaaagtg
65221 gtttctcgag ttggaatcta ctccctggta agatgctatg aacattgtta aaattacaac
65281 aaaagactta ggatattaca taaacttgat tgattaaagca ggaagagggt ttgagaggat
65341 tgactccaat tttgaaggaa gttctaccat gggtaaaatg ctgtcaaata gcatcacgtg
65401 ccacagagaa atctttcata aaaggaagga tgaatctatg cagcaaactt cattgtttta
65461 ttttaagaac ttgccagccg ggcacggtgg ctcacacctg taatcccagc actttgggag
65521 gccgaggtgg gtggatcacg agatcaggag atcaagacca tcccgggtaa cacggtgaaa
65581 ccccgctctc cctaaaaaaa tacaaaaaat tagccgggca tggtagcagg tgccctgtagt
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65701 gtgagccgag atcgtgccat tgccctccag cctagggtgac agagcgagac tccgtctcaa
65761 aaaaaagaaa aaagaaaaag aaagaaattg ccaggctggg tgcggtggct cacgcctgta
65821 atcccgacac tttgggaggc cgagttgggt gggtcacctg aggtcaggag ttogagacca
65881 gcctggccaa agtggcaaaa ccctgtatct actaaaaata caaaaattag ctgggctgtg
65941 tggcacgtgc ctgtaacccc agctactcag gaagctgagg caggagaatc acttgaaccc
66001 agtaggtgta ggttacagtg agccgagatt gcaccactgc actccagcct gggtgacagt
66061 gtgagactcc atcaaaaaaa aaaaaaaaaa agagagagaa attgccacag ccactccaac
66121 tttcagcaac caccaccacc cccatccgtc agtggccatc cacatcaaag caacatcttt
66181 caccagcaaa aagattatga cttgctgaag gctcaagtga tcattaacat tttttagcaa
66241 taaagtattc ttaaattaat gtacttaaca ttttaaaaat acataatgtt attatgcatt
66301 taatagacta cagatagtat aaacctaaact tgaaaatata tggagaaact aaaaaattct
66361 cgtgatttgt tttattgtga tactttattg aagtggctct gagctgaact tgggttatct
66421 ctgatgtatg cttgtaaaatt taacagaggt tatttgagca ttaacagatg tatttatttg
66481 gcagcactta gaactagaaa aggctcagag atgccactt caatagtgtg agcagtgggc
66541 ttctattggc tgaatgtgga accaaagttaa ggaaattact taattgacta cagctgtgtt
66601 gttttctgtg atgggtatga ttttagtaga agtgtccagt tacgttatct gatgtctagt
66661 tggctgttgt ggtagttga agcttgtttt tttttttttt ttaaatttaa tttattacaa
66721 ggaatttttc taaattaaat ttcaccttgt gtaaagttcc atgtacagaa acaggtccag
66781 gctaatttcc tcttgcttat tttgctttaa gaaaacatca ctgggaaact gagttgaaaa
66841 ttaggctact tctggcttct ctgcaaaatc agatacaatg ttgtaaatca tgactgggac
66901 agccttctag acctcattgt ctactcattt tccaatctga attatgttct cctgtgttct
66961 cagttgctta gttcactagc atttttaaat attcaggcga ttgaggaaga ttctgttttc
67021 tttgatagat tgttttatag tctaaaaagg ctgtcaggaa tattttcctt atattcactc
67081 tgaaatcccK tgctcaattt caacatatta catgaaatta tccagataat ctaaacaata
67141 tgtctctgtt cacagtgtgg acatccttta aataatttaa tttctcttta tctctctYgc
67201 tcaatctcat gtttagattg ctatttgcca gtatattata ccatttatgt tctactgtta
67261 ttagagaaat tatattaact aggcagtagg atgtcaggat ttgactattg aagtttttaa
67321 gttttccttg tatttgtttc ctctctatgt agttcacctt gaatacttat attaaacaat
67381 tctttaattg tccattgtca gtctttcata atttaacatc tttttctttt atgaagattt
67441 ctgttaccag agtagtttaa acttttagac tagctaattc cccctttttc ttttaagaga
67501 tagttaaagg aataaaaaaa taaataaatc tgagaggatt tgcggttaatt tcaacagttc
67561 ataccttggg tttataaaat ttctcttttt atacagaaag aatgtacata attgactgtg
67621 ttgtatatta ctaccaattt cacctgatta ttaacctaaa attactttta gttgtcttaa
67681 agatatttaa aacatgcatg atttctaggt tgtaatgcct agattttttg ttggattttc
67741 tctggtctct tgtttccttt tccaagcaat tttatatgtt ttaagaatta gtatagcttg
67801 atgggtgggt ttaaagtaag attgtcctgg tttgaagcct tacatttact ttctttgtta
67861 tttttggcaa gcagatttct taacttgtct ttactttta ttcctcatgt gtaaaatggg
67921 aatagtataa gtatctcttc ttcatagtag ttgtgtttaa tgattacata tatttataca
67981 tatagtcctt gacttatgat gggttttacat cctgataaat ccattgtaag tttaaaatat
68041 tttaaagttg gattaattta atacacctaa cttactgagc acagcttagt gttgctacc
68101 ttttaatatg ttggaacatt tacattagcc tacacttgaa cacaatcatc tgacacaaaa
68161 ctttattttt taataaaatg ttaactatct catgtaattt attgaatacc ctactgaaag
68221 tggaaaacag aatggtcgta tgggtactga aagtgtggat tctgctgagc gtgtattgtt
68281 tttgcaacat tgtaaagtta aaaaattaga agtggaaact ttgtaaaact gggactgtct
68341 gtatattgta agtgcttaga atagtgcact gcacatagta agtcoctcaa taattttaat
68401 tatggttgta ttattattta ttatcattaa attagttgaa ttttgattta tttgaaccat
68461 ataggttaatt acgttttttc atataaaact ttggctcgcc tatgattatt gtttgatttg
68521 gtacataaatt ggttcattat ttgtatttag cattttaaat atttagtgga cactttgtat
68581 gagaatgcag tcttttagtct ggaataaagt ttgctttgag aatttttctg ttacttttgt
68641 gtaggagtgt agctttttgt aagaccctcg ctttgctaga actgggggtt gcttagctg
68701 tgatgcaggg atgtgcagag cctattttcca tgtgacctgt gctcaaaagg aaggtctgct
68761 ttcagaggca gcggcggaag aggtaggttt atttaaacc atagttgggt aacatgttca
68821 caagatatct tttgactcta tgtcctataa taagtgtaaa taataaaaga aattttaaca
68881 tttattctta aagttcttgc caagatcact gttctaaaac ttttaagagta aatgcctatg
68941 agttttgtca gttttaaagc tagtcagacg ttcagaaaa ataattttta tagtgagatc

```

FIGURE 2-S

```

69001   tgacagataa  aatgaaagat  aatccaagtt  gtcttaaagc  attaaaatgt  cggcattttca
69061   gccccatgaa  ttatagttaa  aaaaaaatag  catattttat  acgagaagct  gaaactgtat
69121   ttgggtaacc  ttgctctatt  ttcttttaaa  taaaatcatt  actgtgtctt  tagtatctct
69181   gttactatct  ctttactgtt  acttttaatt  ccataatatt  cttttcagat  ttattggcct
69241   tacgttaaaa  aatcagttgt  ttccagtgtt  tggggactgg  ttaagattcg  ttcaagttat
69301   ctgagtttaa  aactattttc  attacactat  aaaaatgtta  cttacttttc  tgaactctgt
69361   tctttcatga  gtattagtgg  agacttccag  agattacata  cagtataaca  gaaccaccg
69421   aatatagaaa  caattttgag  aatccagcta  ccttttttta  tgtcagttat  ctagacatta
69481   gtatgtaaaa  tgtaaaacag  tgccactctc  ctcaactcaat  ttttgtgtgt  atgtgaattg
69541   tatttagtaa  aagtgtatac  ttcggtaatg  gaccatttat  ttaaaataaa  ttaatgaata
69601   ttgcaaaaaa  ttttcagttt  taatttttaa  tagggtaact  gtctaaaata  taactcacat
69661   aaaccctttg  gagtcctcag  taatttttaa  gaatgttaac  aaattgtgag  caggttcagt
69721   tcattcctta  agcttacata  gtaatgaatg  tttatttagt  aatttttatt  gcacattcat
69781   gatggcctta  tggtaatagt  ctaagcctct  ccttgttatg  ttttttctt  tattgggtaa
69841   attttgttta  ttgtgctgag  attttatctt  agtacattta  tttcatttcc  agaaagtgag
69901   caaagatact  ctgatgaaga  aaaattgtag  aaaaaaattt  gaaggatata  ttttatgaat
69961   aaacagatct  tataggaatt  gtatttttga  tacatgtagc  tgtttttgat  acatatagct
70021   gttccaatct  cttcattttat  atagctgttc  cagtctcttg  attttaagga  Rttgtacttt
70081   gatgaaggct  actagatgaa  cagtgcagct  cttctcagct  actaggtaga  catagagtta
70141   taattatacg  gtaaaagtag  tctggattcc  tcatagctac  aactcaggat  Rgtgggcaaa
70201   agtacgagag  ggcaatacag  gtaagagtta  gaggaccaga  taaatactac  gtaaatactt
70261   ggatcaggga  atctatagga  taaggttagt  tgtctacttc  tggaaaactt  tgagctttgc
70321   ggttagtagg  gtgcttttgg  agccagtggg  gagctttctt  ttttactatg  gtagtttga
70381   ttcctttgca  cagcatcata  tgtcatcatt  tttggcaaga  tggcagctaa  ttaacaaaaa
70441   tgtgtgaagc  agccatgttt  gggacagtgg  ggtgtaatgg  agttatggga  tttggagagt
70501   gcatctccgt  ctaaaggcat  gcaaattaaa  tgaaactaaa  cataatatta  agctacatag
70561   tttacattct  gtggtctgtg  tatcttacct  ataagctaatt  ttgaggaaat  ttacagggaa
70621   acagatacat  taggatgtga  gaattagccc  tgaggcatct  tccttgccct  gctgtgtccc
70681   ttgatttaatt  aggtgggagc  cctggatgct  ggaataataa  aatgcaactt  ttctccctat
70741   tctactacct  actcagtgtg  ctgtgttttt  ggggggaaat  gatttaaagc  atatttacat
70801   atatatgtta  ctggtttctt  gttataaaca  gagaattaga  aaattctaaa  tgttttctga
70861   acgatatttc  aaaaccagga  atattgcatg  aatcaatatt  aatgaagttt  gcatttgaca
70921   gtaatcattc  tgtcttgtct  atttctagat  ggttgtactt  atgtacataa  ggatttatgt
70981   aatgtaatag  catttaaaat  taagaaacac  attttaact  aaaatagatc  tatgtttgtg
71041   agcatatctt  gccttctatt  tccattttat  actctttaga  cactctaggg  aacttttcaa
71101   aagactatat  caagttggat  ttactacttt  ttcatggtgg  ttttatatag  gctgttaaaa
71161   aaaaaagggt  gaaaaataga  ataacatata  cagtttcatc  taatgacatt  gtgtaccttt
71221   ctgtattttt  tatgactttg  tatagccttc  tgacatagtc  ctttatctca  ttgtgagaa
71281   tccatgtgac  atttctattc  tttttcatct  actttgtgaa  tattccagat  ttattaagaa
71341   tagtcaaagc  atgttatgac  acaacatgct  ttattagaag  gatatttaaa  accatgttat
71401   gacacaacat  cttattttta  aaactggact  atagggctgg  gtgcagtggc  tcatgcctgt
71461   aatctcaaca  ctttgggagg  ccaaggccag  aggattgctt  gagggccagg  gtttgaggcc
71521   agtttgggca  acatagcagg  accccatctc  taccaaaaaa  aaaaaaaaaa  aattagctgg
71581   gtgtgatgtt  gcctgtagtc  tgagctacta  gagaggccga  ggtgagagga  tcacatatac
71641   ccgggagttt  gaggctgcat  tgaactatgt  tctcaccact  gcactcagcc  tggagaatag
71701   agtgagaccc  tacctctaaa  aattttaaat  aaataagtaa  aaaaataccg  agctattgtg
71761   caggctcagt  tatgctgact  acaacttatg  ttactatggt  ttacattata  tagtctaaag
71821   ttacttatag  tccaagtaag  ccatattgta  gtttcttctg  taattaaagt  ataatttggg
71881   gctattgaac  attgctgtac  tctgttctgt  agaaaattat  atttgaaaca  atataaaacc
71941   ggggtgtgtg  gcacacgcct  gtaatcccag  tactttggga  ggccaagcca  aggaggatct
72001   cttgaggctg  gcctcaagag  gattttgaga  tgagcctggg  caacatagca  agacccaatc
72061   tctacacaaa  atgtaaaaat  tagccagggt  tgggtggtgt  tgcctatagt  cctaactgct
72121   caggaggctg  aggtgggagg  attgctgagc  ccagaagttc  aagatttcat  tctattagag
72181   catatatggc  tgaggtgggg  tggacaagaa  tattgataat  gcataattaa  gaagataagt
72241   ttgatatgcc  attaggttat  tattgtattt  aaatgtttct  ggtttcagta  aacacatcaa
72301   ttttactatt  aagataccag  taaagcgtag  gtacgttctt  caaatacact  gtttttacia
72361   gtgccaggta  aggttctcaa  tgtacaagac  cgaagttgtg  tcttctttca  gtttatataa
72421  . ctttgatctg  ctatgtcagt  tttaccagg  gagctttgtt  taaaaaaaaa  aaaaagattt
72481   taagattcta  gaccaaatoa  tggcatctag  aggaccacaa  gctaaactta  atccatagat
72541   ggattttgtt  tgttaggagt  agagttaaaa  aagaaaacct  tgaatttaaa  tgactttaga
72601   tggggcattc  cagtttgcca  caggctctaa  gttctcacag  gccccagcat  ttactaactg
72661   cttctcatca  ttcatttttg  tcttatattt  ttctggcatc  ttttaggtct  ccttcacca
72721   tttatgttga  ctattactgc  ttctcaaggc  atttgtattt  aaggcccttg  cctcagctct
72781   gctaagtcag  aatttgcaga  gttgggctct  agttacctct  atttagaaat  ctccttaaat

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FIGURE 2-T

```

72841  gaatctgatg acagtcagggt aatgggttaag gaagatggat cttacatact ggacataggt
72901  cttgggttcag caacttaacc tctctggcctt tcagttttct atccataaaa ttgatattaa
72961  aatggtagaa cccacctcat gtggtagtgg tgaaggttaa agagatagta tatacaaaag
73021  cgcatgtgct tatttcatgg tagatattca gaaacatggt tttcccttct tgtcttccac
73081  tgggagtagg atcttgaaaag ctccattttct ccaagcagggt tgaagggata tttccatgtca
73141  accaatgcat taattaggac attatttttga ctgggttaac aaaaccaagt aacgagttgc
73201  ttaaacgaag aagttgaatt cactctaata tacaattcca ggcggattgg atactgaggg
73261  gagtttggtt ccagggatca gttcccttct tcttcttgc ttcaccttcc tttagtctat
73321  tgcactctcc tacacagtca aagatggttt atcaccatct tgactggatt ctctctcatt
73381  ggaagtagca aagaggagggt taagagtagg cagcttccct tcaaggggcat ggtctgggca
73441  tttcatacaa cttattggcc agaacttaat cacatggcca catctagctg tggggagggt
73501  ggatcagata gtttctagca gggtagccat atgccagta aaaactcata ggggtctagt
73561  actaatggga agaattggata ttgtaagaca attagtagtt tctgccatag taagtattgg
73621  tgtttttctt aagtcagagt cttggtccaa atgcttaact cacctatgca agcatgaatc
73681  ctatctctaa tgactcaatt tcaacctcat ttactttgaa acattagaat aattatctag
73741  atctgggtat ttgggctgag gttcgggtata atctttatct ccatttaaca tctctgtcac
73801  caagatttag agcatgtcat gagaagcag ctgtttgtat gtgtaaatgt agtctcctaa
73861  ttaatttttg tatttaattt ttaaagctat atgaagtaat tgtaagtaaa cctgttttta
73921  ctaatgtggg aactgaggcc cagagatggt aagcaatttt ttgaagtccc atagcctgta
73981  aatgatagag ccaagatttg tatccRgggt tttatgtctt caaattctgt gatacacatt
74041  gctgtactgt gacatctata gatatcacac tacagaattg cctcatatgc ttttttttta
74101  atattaagga cacattagat ttttttttct ttctgttctt atatgtctct cctcggtagt
74161  gttgtcattt ctctttgggt tgtaaaactc tacttagaga cacttttgac ataacttaga
74221  gaaaaactaa tagcttatgt ttactgttcc tttttgggac agacataaag aatgaacagc
74281  ctgttgtttt gttagcaatt acattgtaaa ttactttttt gtactacatc tttacaagtt
74341  gtttttgata gaataaatat tcttttttgt acactacttt ttatgaatga aaatgtactg
74401  ttaggctatg agagagctgt aattccactt gagtttttag ggaaagagtt aagggcataa
74461  cttaaatttt ttatttgaca gggcttagaa tttcttaatt ctattttttt tttttttttt
74521  tttttttttt gagacagact gtgcctctgt caccagcgt ggagtgcagt ggcgcgatct
74581  cggttaatta caacatctcc ctctgtatt caagcaattc tcctacctca gcctcctgag
74641  tagctgggat tacaggcaca tgccactgtg cctggcta at ttttgtactt ttagtagaga
74701  caggcttttg ccgtgttggt caggctagtc tcgaactccc aacctcaagt gatctgctt
74761  cctcgggtct ccaaagtgtc gggattacag gcatgtgcca ccacgcctgg cccttaattc
74821  tattttttat ctcagtagaa tctgtccatt gttagccagt tagaaatgcc acacttatct
74881  tgttggttag ttgaatgttg ttgttttgca atattagttt atgcataact ttaatattta
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75061  atcgaaaaatg tttgaaaaaa aaaaagcgta ataaaaaaga atacaaatat aaaaccaata
75121  cagtgttaaca actatttgca cttttacatt tgtgtattag gtattataag taatgtagag
75181  actgcttaaa atatgtggga gaatgcatgt aaactagatg caaataccac accatttaac
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75301  catggatatt gaagggtac tatacaagta cacccaaata atacattata tttgatttca
75361  atactcttta accctgcagg cctttaaaga aaaacgttgt tggttaattg aagtgtacat
75421  acaagatcaa gtttctaaag aagtaatttt tgtcattatg tacaaaaatt atttttgtaa
75481  tttattagat gtaactagca ctagtagatt ctttgaaaag gaagtaatat tcttttgtgt
75541  taggtctttt atgactcttg ggagtacaaa tgttcactat ttttctgtgc tttcttgtR
75601  taggatatag cagatccatt ctttgcttat tgtaagcaac atgcagatag gttagacaga
75661  aagtgaaga gaaaaaacta cttggctcta cagtcctatt gtaaaatgtc tttgcaagag
75721  agagagaagc aactatcacc agaagcacag gtatgggatt catgtcaaaa ccgtagtgt
75781  tttgttttaa ggttatgtaa ggattttacg tctcgtgtgg cttccagtga catgtgacgt
75841  ataataggaa gtttggttag ttacctagga aatggattgt gattaaggta aatagttagt
75901  ataatttttg gctgaataca gtactctca tttagtcaaa cagagcagtc ctttataaag
75961  taaattttta cattgaaaaa tgttagctgt aggaattac tctatcagtg caatatattt
76021  attacatctt gtttcagttt gttcaaagga tttagtcagt ttgcctatat ttaaaatata
76081  attttatata cattaaacct atggagacaa tagcagttat taagaagaga aacttcagct
76141  taattagttt ctcaaaactc tgattataag ttaggacagt tgttactagg ggcagatata
76201  gtttattgta actcaaaaat tatacagtat accttaagga tcattcatat ctataatttg
76261  ctttggtgtg agaagttctg atttctttt tgtgaacatg ggaataaaaa tcaattgtaa
76321  aatcttaagg aacatgtttc attttattat cttttaaaat ttgaatacat tcttttata
76381  ggcaaggatc aatgcccggc ttcagcagta tctgcccata gcagaactag ctgatctac
76441  cagaccccg gcctgggttc caagggaaaa attgcccaga ccactacca gcagtgttcc
76501  agctattcgt aaacttatgc ggaaagcaga actcatgggg atcagtacag atatctttcc
76561  agtggacaat tcagatacta gttctagtgt ggatggaagg agaaaacata agcaaccagc
76621  tctcactgca gattttgtga attattattt tggtcagtat agacactggt acatgcacat

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FIGURE 2-U

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76681 tttcactgag aacaatttgt taatgaaaat gtttgatata ctgttaattt ttagaaattt
76741 attagccatg ctgcatatat catagaggga tgtttatttt cctaatatgt tgtgggtttt
76801 tacaaaaatgc taggttcatt tatttgtaaa tatacttaaa agtttttaaac tatgtagggt
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76921 agtaaaaattc gatatttcat ttaaataagag agaaatatgc gcatgattca aattcaggaa
76981 aatatggctg acaaaaagaa tataaaagat aaattagaga atgaacaaga aaagcttcat
77041 gtagaatata ataaggtaag ttagctacaa aatatgcaac ataagtgtat agatcttact
77101 gatgatttct tttgtgaatg tatggcattt ctittatgtt ttgttttttaa tttcttctgg
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77281 cccagcttaa ctttatagtg taggttataa tcattgcttc cattttcagg gagaaaactg
77341 aatcctgaag aagttaaata atttgcccag gttcacacaa gtagtcaagt cacagacttg
77401 acaaatgaag tcagttgggt tgaggccaac tcatgtgact ctgttctcta tttctaatca
77461 ataaacattg ctatagagct tcactttcta agttttaga aaatttagaa acttttcttt
77521 aaattattat ttatcttgaa ttatattata atgtttggaa taaaaatttc caaatttgaa
77581 ttttcatgta cctcttcata gtaatgagaa aagattcaaa aagaagtatc ttataaaagc
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77821 agttctgtga tcttggccaa ctcaaaaaa ctctatgata cttagttttt ttcaattggg
77881 aaatagtggg aatacatctt gagagagtca caaggattag ttagcagaac atgatgttat
77941 ataacaaact gtaaaagaag gtataaacgt agttaccatt attagtaaaa atgccagcag
78001 aaaacaaaat gcttacagca acaataactg ctgaataaatt ggatagcctt gtctctcagt
78061 ggtatttggt cttgaatata ttaaaaaat atggaggccg agcgagtggt ctcagcctg
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78181 tcctaggagt ttgagaccag cctggccaac atggcaaaac cccgtctcta ctaaaaaatac
78241 aaaagttagc tgggcgtggt ggaggtggtg gttgcagtga cacaagatcg tgctactgca
78301 aggagaattg cttgaaccga ggcgacagag tgagactcca tctcaaaaaa aaaaaaaa aaatagatcg
78361 ctctagcctg ggcacacatg gtgaaccctt gtctctacta aaaatacaaa aattagctgg
78421 agaccatcct gacacacctg gcacacctgt agtcccacct actcgggaaa ctgcagcagg agaatcgctt
78481 atgtggtggt ggcggagggt gtagtgagcc gaaatcgtgt caccgcactc cagcctggtg
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78661 tgtagatatt aatctttaga agaactacaa aacctgaatg gaaaacttcg aagtgaagg
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78841 catttgacta accgaagaat tctgtttgat cagggcctaa tcctttggga taatgatttc
78901 tgcttgaat acacctagag cattggaagc tgccactga gaacctctag tttaatgtg
78961 ttgtttcaac agctatcttg tgtgcaaaat ttttcathtt gctctaactg attgacctgt
79021 catttgtgat gaagcttaag acttgaagca tgagttttt ctactacatt cttctttcct
79081 ttaatttagc agtttttagat tccctgccac atttttttct ttctgtcct tatgctgtat
79141 ttttttttct attcttttga tgtataattt aaaaataaaa aaggcaaaact agagatatc
79201 atttttatgt taatttgggt ttacgtgta taagagatgg ttttttaaac tttaatgtta
79261 aaatgtattt ttccccttta acagttagct tgatcgtagt tattaaaaa aactttatc
79321 atgaacacct ttagtctggt aaagtttttg gtgttgaata attattgtta gatggatttc
79381 tttgaatgcc ttttttagta ctgtgtatat aattgataaa ttacagtttt cgcaaatatt
79441 ttttattttt taaggatgat ggagaccac tgtttgggt cctttcacta aaaagtagtt
79501 ttatttctga aggagctttt cgaacagata tttttcatta tactgtttt agagtttat
79561 ggagagtcaa attcatcaca cagcttattt aaatatttta agaagtgata catactgatt
79621 tgtactgtgc tataccagct ttgaagatgc tttatgtgaa aagaatgtgt gtggcttgta
79681 tcctaaagaa tgttttaaaa ggtgagaatt agtagtcgcc tctgggagga tcagcctttg
79741 ttcctgttaa taggttggtt gatggatttt tggaagatta tgttttatac ttaatattta
79801 gaggagttaa tgttgagtat aaggcttttag tttatttgcc aagctagcat tatcttttg
79861 cttgatttgc aagtttttct tcctgtttta tccgttttga gaggtttgca aatttccttt tgcaaatgta
79921 acattttcat ttattaaaag acttttaaca gagggtttgca aatttccttt tgcaaatgta
79981 aaatacacag cagaagtaga attcatttat actgcttgca tgacactttt tttttcagtt
80041 ggttgaacag atgtgggccc accaggccac tgagaaatga ctttgataga tggttgctgt
80101 ctgagaagcc agcatactac agatatttag aaaccaagc agaactctac ttgctttgtt
80161 ggagagtttg gtccaataag ataatttttg taattaaact atggaacacc aatatagctg
80221 ggggtgctgaa gaaaataaat ggcctcaata ttctttttgt caagtgtact gtgttttgtt
80281 ttttttaaac ctctacgta tgtgtctttg tctttgaaag ctgaaataga agtttaattt
80341 ttatgtttta gtgtaccact gaaaattgat gaaagtctgt aattatagat ttctaattga
80401 aataactatt agaaaaaagc tcattttaat cctttttgcc aatgtaaaa ctgataaagc

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FIGURE 2-V

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80521 agattttcccc ctaacaatcc tactatatatt acttggccttg agtggcaatt agaggaaaat
80581 gttgcttttta tttcttttctt aaaacaatat atactacatt tgttcaaatac aatagaagtt
80641 gaatataccg gcaatttttgc gagcacccaa ggagagaaaa ccaagtaaaa aagaaggagg
80701 cacacaaaag acatctactc ttcctgcagt actttatagg caagtaatga aattaataat
80761 gatagaataa tgttgtgtat ttttttaaac tgatacttat tagaaaagaag atctctgcaa
80821 tattttgagaa tgaattatgt ccataccaga atttaagtgc atttgaagtt cattttctca
80881 aaagatgcat tccagtttga atgatagagg agatttttgt tgctgtttta acctaaactc
80941 tatggaaatg agcagtaccc tttggggaac tggaaaatta ctttagataa cattatagtt
81001 attgtcttaa ataatttaa caatataaaa gatgagcatt tatattttat tttacttgaa
81061 tgaattgtat agtttgtttt ttatagatgtg atgggtatca tatatgtata tatatagaat
81121 gaatctattg cctttgtagg cagtggataa tgaagataag ttttagtttt gagtttctac
81181 acttttttct tcttgatgct cagttgcaat cactttgttc gcataagtat tttgtttttt
81241 tactttcttt gctcaatatt ttcggtgttc accattatag taatttttatt atagtcaaga
81301 ctctctttcca taaataaata gggtacgac tcactttttc ccaaataatt atattaagtg
81361 ggagaagttt agaagatgct ggtgtttttg tgtgtgtgtg tgtgtgtatg tatgtgtgtg
81421 tataatttata tatgtatatg catacatata tgttatgcat gtgtaaatac ataaatattc
81481 ttctcaaaat ttctttctca gaaatagtag caataacaac aatatcaatc tccataacta
81541 ccttctgttt ttttgttggg ggctccctct acaagtaata gcaaataact tccttgaagt
81601 gtgggaaaag cctacattgt cttagtgtac aatgtgaaca ttagcacatt ctccaggcag
81661 ctttttcaaa caggttggg tcatctggaa ccatcaggca atatcactat gctctgact
81721 tttatgacta caattcattt ttgtttcaga atatatttta agtgattttt cttttttact
81781 gagaccaggt actggttatt tatttattta ttttggcttt ttaagtgtgt gtgtgtgtgt
81841 gtgacttttt tctaggagta tttaaaaaaa aaacctaac atcattgctt tctgtacttt
81901 ccaaatataa atatacttta gattttcagg tgatgggtgt tgtgtacgca ggtgtagtta
81961 aattgccttt ttgcataaga gaagtttagt ttctgagaaa ccaaagatc ctaaaataat
82021 agtagcaatc acaaaattcc acaatctttg caataaatat caattgatgt gtgcgttttt
82081 aattttttta cttttgaatt taattagtat atttttaaaa cgcaaaattc agtattgaaa
82141 agagactcat gtatacttgc agtatatcta catgttgaag actgtttgaa aggtttacaa
82201 ctaatggtag gaaataaaat accttctgtt tgtgaagtaa tttttttata gttttagaaa
82261 attggaaaat tactttgttc tataattttat gtgtctagag aaaaaatgaa ctaatgtgaa
82321 atgggtttta agtaataact aaaattaaaa tgaatatgat gttgaggata aataccttat
82381 atatgtaatt ctttagaagg tttgactcta gtagtattta aatttttacc agatccaagc
82441 tatttttaac attctcaaaa gtattttagaa ctaacagtta ctgacattgt aaaaagatgt
82501 gttaatgaaa gaaattgtct atctcaacag aagaaatagt aagttaaato aagatgaaat
82561 tttgtaaagt gaaaaatatg ctataagtaa actgtttcac tatgataatt attattgaaa
82621 tctttacttg ctgcctttat taaaagttgt gggatttgta agaagaacca tgatcagcat
82681 cttcttttat tgtgtgatac ctgtaaacta cattaccatc ttggatgtct ggatcctcct
82741 cttacaagga tgccaagaaa gacccaaaaa agttatttgt gagtaaaaaa gaggagattt
82801 agatgtttga attgatttac tcttagtttc agcagtataa gatgaaatac tatattgttt
82861 cataataaag tatttggcac attttaaaaa tgactgtcat caatatttat tatagcatta
82921 tgtgactaaa tctataacag cttttttgag aaatgagttt ttcattaat gtggctatta
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83041 tttattgttc agaatttctc aaatgcttta ttgttatttt gaaattgaat ttacttaaaa
83101 tttgcctaca tattatgctt ttactttcaa tttaatattt tatttttggg tagagtcaa
83161 aggettact tctggtattt ggtatttgtg ctagtcatth aaattcaacc attctttgac
83221 atctagaaac atttgataaa catttctgat tttttttttt attaacctag gcatatcgaa
83281 tcactacatt tgataaaggt ttcagatttt aatagaatga tttctcatag gaaggagaat
83341 ctccaagaaa gggacagatg gaatgaacat gaattattct tttatacaag ttacctttcc
83401 ataggaaaag gaaaactttg cccaaatttt taaatggtaa tctctacaag aggttgtgtg
83461 agtttttagaa aagagtgaac catatttttt gacctattg ttttatcact taaggctacc
83521 tgttctctca atacattagg gctgaaattt tttcactatt ttcacatgat tgctttttta
83581 tctgttcatt tgattaggaa tgtttttgag tattcatact ggcctgttct tttgaaatgc
83641 tagtgttctt tgtatcagtt gttttttatg gcttcagaaa ctgctatagc atttcgaat
83701 agtggaatgt ttaataagca tcctgggtga gtttttaaat tgaaagctag tttgatagtc
83761 cccaacaatg tccagagcca ggatgttttg ccatgaactt atatagagtt atgcagttct ctccttaaat
83821 gaagttatgg accctcctga tactgtctcag cctgcagagc tctggtttcc agcatgtgag
83941 agtttctgca gctaaaaaaa aacacacaca aaaaaaggga aatcatgttc tttgtagcaa
84001 caaggaggca gctggaggcc attactctca gtgaattaac ccaggaaaag aaaaccgaat
84061 actgcattgt ctcacttaca ggtggaagct aaacactgga tagtcatgga cataaagatg
84121 gggcctacta gaatggggag ggaggggagc aaggtttgaa aaactgttgg gtagtatact
84181 cactacctgg gtgataggga tcattcatat tccaaacctc agtatcatgc agtatacca
84241 tgtaacaaac ctgtgcatat accccctgat ctaaaaataa agttgaaatt aaaaaaaaaa
84301 gaaaagaagt aatgtacata gcctgaggtg ttttagtgag agcacttcta aaagggcgta

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FIGURE 2-W

84361	aacaacttag	agccttttca	ttgttgttag	tggtttttaa	gtaaaagtag	aagttaatgt
84421	tgtagcacag	tgaagccttt	aatttctcct	tgtttctagt	gataacattt	cctttggcct
84481	ctaagatcaa	cttagccttg	gttagcagtt	aactgggtgt	attaattttg	gagtgtgcaa
84541	gattcagaga	attgtttttt	ctttagtgtg	cctcaaatgt	gggaggcagt	ttttactttt
84601	tgctttttta	catttttcagt	ttatttttga	agttatacta	aagataataa	atactcaaaa
84661	cttaacacct	tctaaatatt	ttgtcacatt	ttactattat	ctatgctcta	gagggtattt
84721	aagtctattg	catctggatg	gtagaaaaaa	aatgataaac	gcagggttag	tatcccttat
84781	ccaaagtgtc	ggggaccaga	agtgtatttg	attttgtttt	tgtatttgtt	ttggaatatt
84841	tgcatgttac	ctactggtcg	agtatcccaa	atctgaaaat	ctgaaatctg	caatgctcca
84901	atgaacattt	tctttgactg	taatgtcagt	gctcaaaaaa	catttggatt	ttggagcact
84961	tcagattttg	gatttttggg	tttgggatgc	tcaacctatg	atagtgtgta	ctacacaccc
85021	ttttcccat	cctacattct	gtgatgccat	gttgataaatt	tgaaattgaa	attgccatag
85081	ttaggagtat	ttgtactgta	gaaattacta	aatactacat	aacagggcct	tccccagag
85141	ggtcaagtgt	tagacattta	ctagcatatc	actgactgat	gtctgcttta	gactctacct
85201	tgttcttact	agtccctttc	ttagggaag	ggtcccttaa	tttctccttg	tttctagtga
85261	tcaaatttcc	tttgatcact	agggtcctgt	tactggactc	ttatttcatg	actgtgcctt
85321	agtctgcagc	ttgaacttcc	acaggtccct	ctggtataat	atttctgaat	ggcgggttta
85381	tttttgcctg	ctttatgttt	tgcaagcctg	tggtagcacc	cttactacta	aataccctgt
85441	aagcaaacgt	tacctagaat	taattactat	acaatctggt	gccttctcag	atatcatatt
85501	ctactcta	aactatttta	agcacttgct	atccagcctt	ttcttccagt	accagcactg
85561	ttttcaagga	gacactagtt	ctagatttgg	atgctttctt	cagtccatcc	cagagtctctg
85621	tggactgtgc	tgggcagggt	aagacatgtg	acatcaaaga	aaagatggat	acagatacag
85681	aagtaattat	tgggtgaagg	taggggaagt	gagtgaattc	accttgga	ggctcagata
85741	tttcagtgat	ataggagtct	Rttgagagg	aagagacctg	ggatgatgat	gggtcttga
85801	gaagacagca	gatggttgg	aacaacttac	tgtggaaaaa	tcaaactgac	ttgctgaggc
85861	tgtgtagcaa	gaatgtttag	tgcataagta	aatgtgatta	tttgattttt	cttgaattat
85921	gctctgctgc	ccaggagaag	gagaggggaa	aacctagggg	cttcttaggt	tgggcccagg
85981	atgtgaaaag	ctagtaaaga	atattattaa	taggtgggtg	aagaattcca	cagagaatag
86041	agaggctagt	gatggtgtga	tctaggttct	attttgtttg	tacctctttc	tagtatttta
86101	aatgcatttt	gtctcatttt	tagtttatgt	tattttgatt	tttgttgttg	tttttaaaaa
86161	tgtacaatct	ccacactgcc	ttaaattcta	agacacattt	ggtaggatac	aatggtaag
86221	ggcttgattt	attagagtag	ttcaaatagt	taatcatctc	ttaattttag	aagactaatg
86281	ttatatttct	gcctccactc	atctgattgt	aacttgtgtt	gcctttttcca	attgtttgaa
86341	gaatattctg	aaacacatta	tttaacagag	aattgagtaa	tatatccttt	tattccttgg
86401	atatgtcttt	attttatgat	gaaaagaaaa	ctcaaaccct	tctaggaata	gtttacagag
86461	ggttttttcc	tttgtttttc	ttgataattt	gttcattttac	atttttttat	tgcctcttct
86521	tcccatatac	cgctagtagg	aattccagca	ttagaatggg	acatttactg	tatatgaaat
86581	aacagggtata	tatctgctat	taaagttttt	acaggtatta	taactacaaa	aagaataaaa
86641	tttacaagtt	gagttaaatg	ttgttttctg	cccttcaaag	agatacccat	aatgcagaag
86701	taggaggggac	tgagggtatta	cttgtctgag	aagaatgata	tttgagccac	ctcttaaagt
86761	tttatgtagg	cacctgtcaa	gactttctct	taaatacagg	agaaaacatg	gctaaccggt
86821	tagacataag	aaaaaaaaaa	actctggtgt	gggatcctga	gttcttgatg	actgaaaaag
86881	ataaattgtg	gaggagaaaa	aagtaaatca	tgaattattt	ggaatatgga	atgttactgg
86941	atttattttat	tgcatatttg	catttaaaga	ttcataaaat	cctttttttt	tttaacttac
87001	acgaataaaa	ttctctaaat	tagtccactt	tctttttttt	ttcttttttt	gagatggagt
87061	ctcgtctgtg	cacccaggct	ggggtgcagt	ggcacaatcg	caactcaccg	caacttctgc
87121	ctcctgggtg	caagcaattc	tctgtcctca	gcctcccag	tacctgggac	tacaggcgcg
87181	tgccaccacg	cccagcta	tttttgtatt	tttagtagag	atgggggttc	accgtgttag
87241	ccagaatggg	ctcgatctcc	tgacctcatg	atccgcctgc	cttggcctcc	caaagtgcctg
87301	gattacaggc	gtgagctact	gtgcctggct	taaattagta	cactttcttg	tctaagcact
87361	attaaacatt	tttcttttag	aactaagatt	ctgaaattcc	attgggtcat	cattctgatt
87421	atagggttga	gttgtatggt	gctagaacaa	tatagaaggt	atagaaaatt	gagaaaaggc
87481	cagacgcagt	ggctcatgtc	tgtaatccca	gcactttggg	aggctgaggc	gggaggatca
87541	cttgaggtca	ggagttcaag	accaacatga	tgaaccctg	tctctactaa	aaatacaaaa
87601	attagctagg	aatgggtgatg	gggatctgta	atccctgcta	ctcaggaggc	tgaggtagag
87661	aattgcttaa	acctgggagg	ctgaggctac	aatgagctga	gattgcgcca	gtgctctcca
87721	atctgggtga	cagagtga	ctctgtctca	caaaaagaca	gaagaagagg	agggaggggc
87781	ggaggggagg	aaagaaggaa	ggaaagaagg	gagggaggga	gggaggga	aagagaggaa
87841	ggaaggagg	aaagaaggga	gggaggaagg	aaggaaagga	agggagggg	gagggagggg
87901	gagggagagg	gagggagggg	gagggaggga	gggaaaagag	aaaaacctct	tggtatttca
87961	acatgaaagt	tattctgttg	cataaattcc	tgacatggat	ttttattata	ctttaaattt
88021	tttaattggct	tggtatcaatt	aaaagggttaa	gattatcttc	agtattgtcc	atgggaatta
88081	taaatttttag	gactctattc	tcatacagtg	tgctaagtaa	aaatatatag	aattaagggtg
88141	agtttagcta	aattaataga	taatagcagt	ttagtggatt	attgaaagaa	gccagggtatg

FIGURE 2-X

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88201  tattttgactt taggaaagat aatcatgatt ttccttaaaa tattatttga tttcagctgg
88261  gcgtggtggc tcacgcctga aatctcagca ctttggggag ggcggggcag gtggatcacg
88321  aggtcaggag ttcaagacca gcctggccaa catggtgaaa ccccatctgt actaaaaata
88381  caaaaattag ccaggcatgg tggcaggcac ctgtaatccc agctactcgg gaggctgagg
88441  cagagaattg cttgaacccg ggagatggag gttacagtga gccttagatc atgccactgc
88501  actccagcct tggcaatagt gcaagactct gtctgaaaac aaagaaaaaa taattatttg
88561  atttcattga attagacagg ccattggcttt attctagggtt attatttctt accatcttgt
88621  gtaccaatta atgtagcaga aacatttttt acatatctta aaggatattt ataagatgaa
88681  gactatagtg tttaatagat tgttgaagaa tggctaagaa gtattatgtc cataatactc
88741  ttgtagtcta ctcagtgtag gtagatggag ctgcaacaat catgtggcgg ttgtcttgaa
88801  ataggaaatg atatatcttg cattggcagt tacatttgtt ttgatttttt gagttgttcc
88861  gtgttttgtg gtgttcaggg tgtaacattt ctattttctg ggaattagcc aaatttcttt
88921  gtcacctaac tattatttat agtggggatg gaagtgaaca taagaataaa gaatgtcctg
88981  acaagggtaa ttgctaccaa aagagaagcg aagaggaaat atttcagttt ttaaaacaaa
89041  acaaaacaat gatttatctg aaaaggtacc tgcttctata cctaggggat ttagataaca
89101  ttatgtttgc ctgttattta agtagacaaa caacatattt taaaagttaa ttagagcctg
89161  gcgcggtggc tcacacctgt aatcccagca ctttggaagg ctgaggcggg aggatcacct
89221  gaggtcagga gtttgagacc agcttggcca acatatagtg aaacctgtc tctactaaaa
89281  aatccaaaat taactgtgcg tgggtgcaca cacctgtagt cccagctact taggaagctg
89341  aggcaggaga atcgcttgaa tggggaaggt ggagggtgca gtgagccgag atcggtccac
89401  tggactccag cctgggcgac ttagcaagac tgtctctcaa aaaaaaaaaa aaaaaaagtg
89461  taaattagaa ctgtttgaga aactgactac atttcactca actgatagaa atgatcagtt
89521  agcattaaga ttacaattta atgtgaaaa gtgaagcagt gtgccttttt gtaataataat
89581  atgataattt ctctagtcac ctgttttgaa ggctgttgca tttattatta gttactaac
89641  aatatctaac atttctgggg ttttcacagt tctgctaata aagtcagaat atacttatca
89701  tttcaattct gagattctgt aaggtgtgta ttttcttttg ccagtccttg atgttttcat
89761  atgggacaaa tgcaggagca atttaataata ttogtttagt tgtgtctttg ttaatgatgg
89821  taatctgaca acctagggga taacctgcc aactatattt catgaagtgt agcaatagat
89881  acataaaagt tttctgagta atacatgatt atgtacattt ttgttttgct ttoactgatc
89941  agtatttcta tgtgctcaaag ttttgctaac ctattcttaa ataattggaa attttaagat
90001  atttaaatga atacgttaag gattaatttg tatttttagta ataatatgtt tgcattaaca
90061  aaacaaatgg tacttggtat ttaactcttg ttggagttca aaatttaaag ctgtcacttt
90121  gacaattaaa tattagttta ataagttcac agtattagtg aaagatgtga attttgatgg
90181  aacgaaatca aatcataaat ctttgaaaa acttgctatg agaattataa gttacattca
90241  aagatactga tataaacata taaactaaat atcaaataca attttacaga ttataatcat
90301  ttttattaag agaatactat caaacttttg gagaatttgc ttttgatcat tcttttacat
90361  ttgaagaaa tatgagtaaa aattttacttt taacaactgg ttttaacttt ttgaaatggg
90421  cctttatgat tgacaatata aagattttcca gcagttgttg tttagatttc tgctgtctaa
90481  atgttagcca ctagccacat atggctattt aaatttaaat caattaatat taaaatgaga
90541  aattttctca gtggtatttg ccacatttca agtgtcagat aacctctat ggctagtggc
90601  cactgttctg gacagcacag atatgtagat aatcctaata ttataaaaag ttctgttga
90661  taccacttgt cttaaagttt agtttcaatt aatttttaat attaccata ttaaaattct
90721  ttataaatgc tactttaaca aattcctttg ataaataaat gtatatttct tcttttagaa
90781  gtagtagggg ccaccaaMta atatgacctt ttttttcccc caacacttct tggagtctgt
90841  ttgtatagtt tctttaagta gtatattcag cacaagttgt caYtgactac aattaaaaga
90901  tatgataact gtgacaagga gtagtgtag ggtccttgaa ggactttgat tttcaggtat
90961  cacagtatat gtcattttaa gaaaagtcac gctttccaaa ggtaaattat tattattatt
91021  taagacaggg tcttgctcat gttaccagg ctggagtgc gtgttgagat catagctcac
91081  tgcagcctcc acctoctggg ctcaagtgac tctttcactt cagcttctcg agtagctggg
91141  attataggcg tgtgccacca agcctagtta attttctttt ttttttttg aagacagtct
91201  ctactatgt tgtgagcagt catcctgcct cagtctctcg aagtgtctgg attatggWg
91261  tgagccactg cagctggcaa aaccaocttt ttaatcagtg ttgaatctca tgttggttca
91321  cttaaacata tagcattgtt aaatgtgttc ttatacttac aggatacatt aaattgcctt
91381  aaattattata ttcatagtag tcaactcttg aggagtattt ctgaatgttt tttcattatg
91441  taccctataa tcacattacc tgtgtatatt tttatatatt attcttatat acctggattt
91501  tgtattttata aaaactatag ctaaagccag aagataataa taaatgcatg acttaaat
91561  ttccctttta tgtaggcagt gctcggaatg tgaccaggca gggagcagtg acatggaagc
91621  agatatggcc atggaaaccc taccagatgg aaccaaacga tcaaggaggc agattaagga
91681  accagtgaat tttgttccac aggatgtgac accagaaccc aagaagattc cgataagaaa
91741  cacggtagtt tattttttat ttatcataag catcatacaa ttctgaggcc aaaatttaag
91801  agagtgaagaa agacacaggg caaacatata ctcagaagtc aaagaaaaag acatctattg
91861  gttattctta acaatttttt ttctatatata tgaaatatac cacatgctta cctgagtgtt
91921  tgtagtttat attttgttgg aggcataata taaggaaacac accagagcat ccatcaccca
91981  ccttgaaaga cagaccattc ccaaagcttt agaagtttcc cgtaaacccc tcgacaagct

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FIGURE 2-Y

```

92041 catctttatc tgtctagccc agaggccacc tctttactca gctttacttt tctcattcac
92101 ttctttttct ttatagaaga gatttacact ctaaatttct gtacttataa ataatacatg
92161 gttttattttt gtaggttttg aatttcatat gaatggaatc aaatgttttt ctctggtaat
92221 ttgatattttt gacccaaaatt atgttgattt gattcagaca tgctgatcca tgtagtgtga
92281 gttttatttat tgtcactaat gtatagtttt ctatggaaa gaaatagattat tacctagttt
92341 ttcttttgct ttgttgatgg gcagttaggt ttttttcatg tttttctatt ctatacagct
92401 ttgttttaaaa ttttctata aatatctcct gcagcatggg aacaaggagt ttgtgtatgt
92461 attaagggtgt agatttgcta agttacagac tatctgcatc ttcagttttg ctagataact
92521 gcaattgttt tccaaaccag ttcacactca taccagcaat ggataatgtt tctgttgctt
92581 cacaaagttt tgtccagtg ttaaatgctt tccagtggtg tacagggaaa atagtatctt
92641 gacattttat gttgcatttc tctcagttat aatgattttg ttcattctatt tacatatttt
92701 ttggtaaattg ttttctctt tctgggaaat gtgtatgcaa gcctttcacc agtttttctg
92761 ttgggggtgtt tacctttttc tcattgcaaa ttttttgagg ccaggtttta aagagtttct
92821 tctggggaaa tcatttatgt tcatgtttac caggtacctt gaaggggcct ctaccaactt
92881 gagaatatttt taaataaaa tttgtgtgtg atgttttcta ttacatcagg agtgtaaatt
92941 tcaaaccttt aagtgtggc ttacagttat gaattcttag ggcatacttt ccttgcttga
93001 gctgaggcag gcacttttca aaaatcttcc tttccacaag ggagatacaa agatattttt
93061 aggggttagtt gtcattctt gttctgttac ctgtttcatt ttaaagagtc tttatatttt
93121 tccttaaagt aacagttttc tcaaaaaa ttttctta ctgtattaac ctctatat
93181 ataactcatt aaaaatctt attcaggaga ttcagcttga ttttttaaat cagttttgtg
93241 ttatggggtc atataaaa tttatggcaa atctttatct cttagataat tgaacaggtt
93301 tttttgggt gctctaagta gatcaacttg aaatagtttt tatttgtagt tccaactggt
93361 tataactctt tttttaggct tcaaaaaa attttgttta taagggaact agagagactt
93421 ttctttgtt aaataagccg gctagtttct atttctaaaa ttttttctat aattggttga
93481 aaatggtaac tagttattct taagatttta gagaagagtt attacttctg atgtctgtct
93541 acaaagatta tctctttatg aaacattatt tttccagttt ctttattggt tcaagaaagc
93601 cttttgacta gtattatcat ccttaacttt ggagttatca tatagaggga aattatgtat
93661 attacagtga aattttttgtg cccacagttc agtattactt gagataaaa agaaactctt
93721 aacattaaag gatccttcta tttttttctc acccttactg gtctgctttt tttatcttag
93781 aattataaag aagcttttaa atttgcta ataatccat tcctttcatc ttgttctttg
93841 tctctagttt tcttgtttaa aagtttttaga cttcttacag attttggtca gtgaaacacc
93901 agggaaagag tccatgacca gtaatttcag gaaatgcagt gtgattattt tcttacttgt
93961 agaaattcca atgcatgttg aagctccaaa aaaaaaaa cctaataattt agaaacagga
94021 ttacttttat ctattctttt tcttaacttg tttttatcaa aaaagcattt ttttaagcac
94081 tttttttttg gtagcataga gtactgtgtg gtgctaagtt tggaaatgat gctccggaga
94141 ccatggatta cttgcattag gaccatcttg ggtatttggt gaaatgtaga ctttgagccc
94201 accctagagc tagtatagac tttggaccca ttctggaatt aatcaattag aatttagggg
94261 tttgactaag cagatttctt aggtgtctac cttatactaa ataaaagtgt aaaaacta
94321 attatgggtga ttacctttcc tttttccctc tcatcttttc tgccctgcctt ccaacaatcc
94381 attcagaaaa ccagacaatt ggtgagaggt atcactacta actgttcaag gaatgtagga
94441 atgagagata cagaaggag tgatcagtc ttttgggtct gatcttacca tttatgctga
94501 gttcctgttg ttaccttaag tttttactta tttctatttg agttgtattt atctttttta
94561 atcaataggt ggtatggtga aaaaatgaggt gttctaattg tgtttcttag aacagtgtta
94621 attatgagag accaggcata caacagctta ctaacttgta taaaatcctt ttgcaatata
94681 taactaattt ttctctccca ttgttacatt tttaaactat tgctcccaat atctctctac
94741 ttacactttt atttcagcac aggtattaca attgggaaca ttctgtcttg taatacatta
94801 ttatagtatt tttatttttg tcagtttttc atttttctct ccataaattg atcaaagtat
94861 aatttgtttt catgttagtc ttattattct gtcattgatt tgaagaaaat tttaccttca
94921 tgacatacgt agggcaatca tgacataccc caagctcatg gacctgaact cctggcagac
94981 agcaactgcc ctgtttacca cagaagaatg ggtcccatc ttcttatgtt tcatcagtga
95041 aactatagaa ttattgtaaa ggcagcctga gatagtctg ttttaagtact ttgttattta
95101 gacattttct ctgcattatt tttctatgtg aaacttttac ttacttttag gcaaggaaat
95161 taattttgaa gaaaacataa attagcttac ccataccct tttgaagtta ctttaaaatt
95221 ggtgtttata ctgttgaca tttttcttaa tactctaag taacttgaaa gctttcagat
95281 tttctttttg ctttctttgc actctaagtc atgtagtgc ttttcatctt ttgtagaagt
95341 gccaaaggac ttgttggtgac ctctctttcc attgttttta cacacacgca tgcattctct
95401 actctctttg aagttstgag atctttcttc ctgacttaca aattcKgggt gtgttttata
95461 tatttttctt tttgcaaaa atatgcaata aataggcaaa atacttttta gcagcttga
95521 ctgaaaacca tattgttttt caggatgcac tatttctttt agatcattat tttagaagga
95581 gatttaaaaa catctaactg tttttccatc gcacttaaca atgtgagcca ctagccagtt
95641 ctaagtggca gtctttattt gagagataat caaatatcct agagcctact tttattacat
95701 ttatgtttta actaatttta cgcatataca aagtacctat ttaataatgt ttaagcttaa
95761 gtcttgagaa tctgaaaata tgaaaatagt ttcataataa ttttttttag atgttagttt
95821 aggaaaaatg ttgaagcatt tggattcagt tctactgaag tgactaaagg ttactgtaca

```

FIGURE 2-Z

```

95881  ttatgttcat atttatttta cttattctta tactaactgt ttgaattact acagttctgg
95941  gaaagaagag ttatttgtgg gggctttaca taccagagtt ttctattatc agactcaagg
96001  tgacctctga ggtacgagtc agattataaa acctctatct gtcatagatt cttagaagaa
96061  accctggcaa acagtttttg tagtgaacta gaactcactt tggctacttg gaagagatct
96121  actctgtggg tgtccttagc tcaagtaatc ttattcagaa ccctgagact cctgttttgc
96181  tttttgcctc ttggaaatcc atcactttta tttattccca ggagtatgaa ataaagataa
96241  gaataggtgg agctttcaag actttccctta ttttgtatat accattatct ctgagaaggt
96301  ttttatagca gcacttactt gtcatgtaga atacatattt tattatatat cattagacct
96361  atagttaKtt cagtttatag tagttaagac aaattgggtta tgattttctt tttattctcc
96421  catatatttt cataaccctg ttaacataag cttaaattaga taaaaagaaa ctctacagtc
96481  aattgaccda agggaaagca ctcacttttg gtgactgcc a ttccattggg tgtttattgg
96541  tagccaacag aaacagatga caccttggtc ataatttggt ttttgtatat agcaattttc
96601  tttgaatatt tcatgaactt taacttggtt tcaatgcagt ttcataattg aaagacaaat
96661  atttttagga attatgtata tgtataattt tatatttttt agaaattata tttttattat
96721  atattgctac atataatata tgctatacat ataattttat attccttagga attaaatata
96781  tatttatatt ttatatatta gaataaattt tatattgaag catttttgaa tagctgccag
96841  aaagctactg gcatttattc cccagcataa atctaattgct atttagctta acagaggttt
96901  tcaaagtttg acttaattgt cctaattaac attgattttg gaattttgcc catgaataag
96961  catgttctat ttttacatat aagttgcaga gggaagcatt tcttatgatt caccatattg
97021  aacttacttt aattattaat ttgtataaaY attgatattg caacaaaaac caaagtgtta
97081  aatttagtga cctggtcaca agtgaatatg tgaagcctag tttactgata tcaaagatgt
97141  taaggtactg actcttttag ttttaaatat agttcatttg ccaaataaat catgcatttg
97201  acttgattgc aaattaaaat aacctcagct ctaaagaatt aattaaaata cattacatgt
97261  tttttagtcc aaatgataga aaagtttagag aaatgtttta ttatttgttt tagatgaata
97321  aactatttat ttacttattt ttatttttat ttttttgaga cRgagtcttg ctctgtcgcc
97381  caggctggag tgcagtgggt tgaccttggc tcaactgcaac ctccgcctcc caggatcgag
97441  cgattctcat gcctcagcct cctgggtagc tgggattaca ggtgtgcacc accacgtccg
97501  gctgagtttt gtattttagt agagatgaga tttcgccatg ttggccaggc tggtttcaaa
97561  ctcgttacct caggtgatct acccgccctg gcctcccaa gtactaagat cacaggcctg
97621  agccactgtK ccggcctga ataaactatt taaaagttgc ctgctagata agataatttt
97681  acaccttttc agtttaaaata cattgtctct aataccatgc caatctcttc tatggatttt
97741  ttaatcacct cttttcaagt aagttgatca cggacagatt acgagcaagg tgatttaagc
97801  agctcagggt gtaattgttc cctagctaaa tcaagttctt aaaaaaaga aaaacaaaaa
97861  attggaatgt gtcaagattt ggaatgagtt ttaaactttc atttactttt aataggttag
97921  ctaattactg tcaaaattaa tcagtttgga attgcacct tgcttgatta atcatgtgga
97981  atttccagRt aacgtatctg tgttacattc taaagcacat tcttgaaaag taaaattctt
98041  ccttcttcca catattattt tcatcctaca gttttattgt tgctaaaagta gtttcagcct
98101  caaaatRtat cagaaaagga ccaccagtt atatatactt ctattcatct gagatgggac
98161  aagctctttg gtaactgaaa tttgtcagat aggcccaact tattttcggt tttcttgcct
98221  ttttgtacca tttctccctc ttttaaatc tacttatgtt ttgggattca ttcaagtaCa
98281  ctactttcaa gataacttgt

```

FIGURE 3-A

>14:71227101-71317000

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1      aaacccagag atgttaaaag acacattaac cagttgcaat gtagggttcc catttggatc
61     ctgattttaa ctacaggggg aaaaatgaat gttggccaaa tatttgatga tattaagtc
121    ttatttgctaa ttatttgagc tctgatagtg atttgtagtK tgtttgtttg ttttaagttct
181    ttaccatttta gagatacata acaaaatatt tacagatgaa atcacgtgct tttgtggatt
241    tgcttcaaaa taaaatgagg tcagggagaa aagtaaggag tgcgtataga tgaaacacga
301    ttgacctga gttgaacatt gttgaagcag ggctacatgg ggatgtgttt tactattgtc
361    ttcagtttta tatgaaggty aaatttttcc aaatgaaaca tttttaaaaa catatccagg
421    cagagccaga aaaatcacat tcctgtagct gtctccctaa taaaaaggtc tttattctgt
481    tctttgcagc ctagaagact agtgtcactg tagctgtagt aataacagta atatcaataa
541    taataggcca ggtgcagtgg ctacgcctg taatcccagc actatgggag gccaggcag
601    gcagatcatg agatcaggag ttogagacag cctgaccaac atggtgaaac cccgtctcta
661    ctaaaaatac aaaaactagc tgggtgtggg ggcgcacgcc tgtaatccca gcgactcagg
721    aggctgaagc atgagaatca cttgaacccg ggaggcgggtg agtcgagatc gcaccactgc
781    actccagcct gggcaacaca gcaagagtcc atctcaaaaa aaaaaaata acaataataa
841    taataatacc cagcattttg gaagcacata cttgctatgt gctaaactca ttttaagagtt
901    tttataaatt ttctcattta attcagacga aatcttatgt ggtaagtact attattatct
961    acattttaca gatgaggaa ctaggggaca gaagtttggg gacaaaggta agcctcacac
1021   ccagatctaa tggcagattt ccggccttgta accaacaccc aaaggtaaaa gatgaagatt
1081   gctgtcatgt cctcagtcct gccttctttg ggataaacac ctttagctct ttcactcccc
1141   accccacccc acccctgcca catggcttca atgccccaca ccactcttgt cacattcctt
1201   gaaacacctg ccaggagcca taaaaagtac tgagcttctt taaggtatct cagaggccca
1261   tgtgcagctt gccccacccc gatcctaccc aggcctgcctg gtttccaga caagctgcgg
1321   tcctcctccc tccaggctgg gagcctgcac atgcgcatgt cccaggagtg gcgcagctca
1381   cctgggcttc ggtgcctctt ctocatccag atgtagcagt tgttctgggc caccocagtc
1441   tgtgagtcca ggaagggaag acgcacgctg cgctctgcac acagccgtga gttgtaactc
1501   cggcagtgct caatggcttc cttgtagaac tgggtcccga gcctgccaga gtcagagagt
1561   gaaggggtga ggccaggga gactgaaaca caccagagg gaaacacacc cagagtgaaa
1621   cacacctccc tggaaagact gaagacctcc cagttatgaa gaccaaggca atgagacca
1681   agagccttgc caatgagcag aatgcaactc aatgtcaggt ctgactaga ttttattttc
1741   tatcccaaat ccaccaggca acttagaaac tcctttaaca aagagcatgg gcttccaagg
1801   atgaatcacc agtaagagag agctgtccat gttctaggaa gcatgaggtc ccactccaga
1861   agggaagtag ctctggaaca acottctgca tggaatctag aggcacacac acttctagaa
1921   cctcctcact catattagct acattttatt ctcagagggtc accagcaaag gcactctagg
1981   tgaacccaaa tcaccagcaa agatactcag ttttccatta caacagaaga gaaactctcc
2041   atataacaaa aaactaggac agaaaaaaca ttctataaaa gtagggaaat tgcaggaaga
2101   aggggtgta gaggaacagg caccaatctt ttaaaacccat attacttaaa gaaaaataac
2161   tttccgatag aaaacaaaca gaattcaaca atttttaatt caaaataatt caactcatgg
2221   agtttaaaaa acaaatagaa agacctttct ggtttgctag actgagaatc tgattaagca
2281   cagtatatatt tacgttcctg actcttttgt atttttggac acgtgggtgat gctactaatt
2341   ttaaggtagt gtccttttca aagacaaaaa atggagcatt gatataattg atcaaatgca
2401   aagcctctaa ataatcaatg agatcaaaata cctaccaaatt aaaacatagg caaggtttaa
2461   taaatgcctc aaagaaatac aaatgtaata acataactta tgccaggtaa attcaagcct
2521   cttactgggg tcggggggca gtggacgcaa aggagtggag tgtgggaaga agaagtagga
2581   agggaaggag ccacagagtt cacaggggca aaaggagaa tcaagtgttt attctgaagc
2641   aacattatga tatctttttg ttttggttct atgtagattt cagaaagcca aaatgagagg
2701   ggaagtctct aaaaatatca tttcttaacc aaagtattta gaggaataaa aaaagcaaaa
2761   ttggggtggt ggggtttttg ggtttttttt tttttttttg agatggagtc tcaactccgtc
2821   gccaggctg gagtgcaacg gtgcgacttc agctcactgc aacctccacc tctgggttc
2881   aaacgattct cctgcctcag cctcctgag agctgggatt ataggtaacct gccaccatgc
2941   ccggctaatt ttttatattt ttagtagaga cagagtttca ctatattggt caggctggtc
3001   tcaaaactcc gacctcaggc gatccaccog cctcagcctc ccaaagtgtc gggattacag
3061   gcgtgagcca ccatgcctgg cctcaatttc ttaattgtgg taaaatacac ataacataaa
3121   atttcccatc ttaagtgtac agtttaagtg tacagttcag tggcattaag cacatgcata
3181   ctggtgtacg accaccacta ctatccattc ccagaactct tttcatcttg caaaactgaa
3241   acactatacc cattaaacaa taactcccc ttccgcctct gccccatct cagcaacta
3301   ccaatctgct ttctatctct atgattctga ctactccaag tacttoataa agtggagtc
3361   atacagtatt tgtctttttg tgactggctt atttgactta gcataatatc ctcagggtta
3421   acctatatta tagcatatgt cagaatttcc ttctttttta agtcagaata atattttaag
3481   tcagaataat attttttaag tcagaataat attocattgt atgcataac cacattttgc
3541   ttatccattc atctgtcagt ggatattctg gttgcttcca cattttagct attctgaata
3601   atgctgctat gaacatgagt atacaaatat cttttcaaaa cctgctttc aggctgggag
3661   cagtggctca tgccgtgtaat ccagcactt tgggaggctg aggtgggttg atcgccctgag

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FIGURE 3-B

```

3721 gtcaggaggtt cgagaccagc ctggccaaca tgggtgacacc ccgtctctac taaaaataca
3781 aaaatttagct gggcctggtg gcagacgcct gtaatcccag ctactcaaga gtcgcttgaa
3841 ctCagaaggt tgtggtgagt tgggattgtg ccactgcact ccagcctggg cgacagggtg
3901 agactctgtc taaaaaaaaa aaaaaaaaaa aaaaaaaacc tgctttcagt tcttttaggt
3961 atatactcag gagtagaatt gctgagtcac atggtagctc tagttttcat tttttgagga
4021 accaccatac tgtttttcat ggcagctgta ccattttcca tttctaccaa cagtgtacaa
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4201 tatcttactg tgggaaaaca caaccctgga agcttctgag gcatcatttg gaaattactt
4261 gttgacaagc atccaaaaaa aaacaaacaa aaaaacaaaa accctttgct cctttttcac
4321 ctctgaacat cttcacattc ataagggagg cataatacgc tcagaaagtg tcctggcagt
4381 tgcaaaacca aactgtaatc aaattgtaat agtcacgcag ctggaaatga attggggagg
4441 ggagatgaaa gccattaca atgctataaa actgaatggc acataagctg atgtaataca
4501 agctggtaac aaggatcatg agattgatca aaaataaaga accacttttt acaaagtgtt
4561 tgtgtcacac cagcttaaat gcttcttctc gctatggcga tgtagctcag tggaaacaga
4621 ctttcacagg cagcttggcc cagacaagat gacccaggct gttcagggta tcctggatgc
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4741 acatttgaca gagaggtgtc caactgtaga gcagcaatct gttttcccag gaccttctga
4801 cagactgcc aaaaaaaaag atgtttaatta tcccaacctc agaaattctg agaaagagag
4861 aaccataaaa atcaggcccc ccaaaaaaac aaaatgaaaa attgtatagc aaaactcatc
4921 tactggagat gatcactttc aaaataaatt tctggaaacc aatacaaaag aaatctacac
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5041 tccagacaag aggaacaaga aactgaaact gctaaaaatg caaagtgagg ttggccaaca
5101 ctggtgtctc acaccaactg gatcgagaat gtcaaacaaa gtggcacact gggcgaaaat
5161 taatttcatac ttaaataactt tctactttca taacatgcaa tgttattagt tacaagcatg
5221 ctgggggaaa atgtatatatt ctaaatataa tctttgtgtg aatgatacct gtcttatgta
5281 aacagaaaag actttctgtg gactggaaca actgtattaa agatcgaagc tgcaaaaaca
5341 tgacattcaa cagccctctc accatcatct ccagggaagt ccttttaaac agaccagggtg
5401 ttggcagaga ttcggaacca aaattttaaag cctttttcaa gatataagag gagaaaagag
5461 atttcacact ccctgataaa ttcaagaagc acttctccaa aagttaatta gccaaaatcg
5521 tcacagggct tgctatgctc tctagaagaa aatcaatgac tagttctccc taacccttag
5581 aaagcaattt aaacagcaga ggacaaatgt cctttccaac atgggtatttc tgccaaaaaa
5641 aaaaaaaa atcccacaat gatgggatcc caggagtgc atttacatta aagtgaagg
5701 cgtcagatgg agcagggaag ggctggcagc aaatgactca tctgtggagt gatgaacagt
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6301 gctctcaaga ccacacctgc ttgctccgat ttctcagatc actctcaggt ccaagcagac
6361 acctgggctc ctccctttca ctgtctctct gggtctgtgc tctgacctga ggacagggtg
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6661 cccaagtccc ctttgctgtg taaacaggac cttggcccat cactactatc tgtgcacaga
6721 agcagagata agcagagctg aagagaagcc ctggcctgtg gcaggattgt gggggtctc
6781 cttccccag aggcgcctct tctcactgtg gggcaccaag ttttctctgt gtctactca
6841 gctgttcaca ccgcagagc cgccacaaa cacaacgaa agctcatcta caccaatag
6901 ctaatttctc gctatttgca tttaaacatg tttaactcaa actgttcatg gaaagctcg
6961 tctcccattt agtcttttag aataactggc acacagggg caatatctgg caaggtgcgg
7021 gaaagttttt attttccttg aagtgttctt gttcctaata catctcttga aagaagacca
7081 agtttagtgt ttgttacaga ctgaattgtg tcgttctctc tcacagaaaa aatccacatg
7141 ttgaaggctt aacctcaat gtgatgtgtg ttggagatgg agcatttggg aggtgatata
7201 atttgataat taccctgcc caaatctcat gttgaattgt aatcccaaac tctgggggtg
7261 gggcctagtg ggaggtgttt agatcatgtg ggcacatccc tcatggcttg gtgctgtctt
7321 cgtgatagca agtgagttct tgcaagatct ggtcatttaa aagtgtatgg tgcctccctg
7381 ctgactctct ctctcttgct cctgttttta tcatgtgaca tgctcctcc ccctttgctt
7441 tctgccatga ttgtaagttt cctgagggtc cccagaagc caagcagatg ccagcactgt
7501 gcttcctgta cagcctgcag aacgatgagc caattaaacc tgttctttat aaattaccaa

```

FIGURE 3-C

7561	atctcaggta	tttctttata	gcaatacaag	aatggcctaa	tccaggaggt	aatcagggtca
7621	ggaggatgga	gccctcatga	tgggattagg	gcccatataa	ggcagagaca	tgagcaagct
7681	ctctcactct	ctcaatctct	gccatgagag	gacacaaaaa	ggcagctgta	tgtgagctat
7741	aaggaggact	cttacctgga	atctgaccct	gctagcacc	tcctcttgaa	cttcccagcc
7801	tccagaactg	tgacagacaa	ttattttaagc	caggggtccc	aaacccctgg	gccacagagc
7861	agtaccagtc	catgcctggt	aggaactggg	tggcacagca	ggaggtgagc	tgtgggggtac
7921	aagtggagcat	tgctgcctga	gctctgcctc	ctgtcagatc	aatggcagca	ctagagctctc
7981	atagaagcgc	aaacccctact	gtgaactgca	catatgaggg	atctaggttg	cccactcctt
8041	atgagaatct	aatgcttgat	gatctgtcac	tgtctcccat	caacccaga	agttgtaaaa
8101	tagttgcagg	aaaacaagct	cagagctccc	actgattcta	cattatagtg	tgagactgtc
8161	ttattttcatt	acatattaca	atgtaataat	aacagaaata	aggtgcacaa	taaatgtaat
8221	gcacttgaat	catcccaaaa	ccatcccctc	cccgaaccca	gtcgggtgaa	aaatgatctt
8281	ccatgaaacc	agtccctggg	gccagaaagg	ttggggactt	ccggtttaag	ctacccagtc
8341	tatgccattt	taatacagca	gctggacatg	actgaggaag	tgtttctgga	tgtttcccaa
8401	aaaagggcta	aggaggacag	gtgagagaga	ttccaatccc	ctttccttcc	acattttttc
8461	ttcttctaac	aaagacaaca	ataataacac	tataatatca	atttcaactc	aattcaatgt
8521	ttagtatttg	tcttctctac	tagactataa	actccatgag	ggcagaggcc	acatctgcag
8581	agccactgca	cacagacact	caggctgaac	aactccagca	agtaccattc	acatcagcgt
8641	caatatgaag	gccaccccct	ggagtgggtg	agcccagcac	tcctgcatac	ctgcctggcc
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8761	agtctccatt	gaaaagcatt	tgacaactca	cattccactc	acctagggca	ggcattttaa
8821	ttacagcagg	aaggctaatt	tggcatgctt	gtgcacagtc	tgacagagtct	gtgactggca
8881	atttaaacctg	gatggctgtc	cacttgcagc	ttcagaaaaa	cattgagaga	atgtctgcat
8941	tcactctcct	gtagtcctca	tcacccagca	cctgggacat	tgacgactg	gggtgcctaa
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9061	agtgttttagt	ctttcaaaact	cctcagtgtg	gaacccaaga	tggctcccaa	tgggtgccag
9121	gttccctctgc	tgggctgggg	atgcacccgg	aaaaactatg	tattggggta	aagtggaaaa
9181	tcaagacttg	gaattgggtca	tgtctgagtc	cagctccacc	tcttaatagc	tacacaaccc
9241	tcagcaagtt	acttaccctc	ctggggccta	aattctacta	ctcacaatat	ggtaatatata
9301	atctctactt	cagacctgag	aaaattttaat	aagctagaac	ctctggcaca	cagacataaa
9361	agtctgcaat	caatagccat	tccttttctcc	ttccccaagg	tgacagtactt	gctgccactt
9421	tgtggcatga	ccctctgcct	gagcaggctg	atacccacca	tgtgatgcaa	cactcactat
9481	tgcggtgtcc	ttaggctgtg	cggggaccca	ctcaaaccctc	tgcccaggga	cagaaggcct
9541	ctgggtcacc	aaggctgagc	ctcaggcatc	caggagagca	gggcagctga	ggcagctga
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9661	ctctctccca	aagcctagta	catgctgggt	catgcctgcc	acattgggta	aatgatgaRt
9721	gaatgagtg	atgaatgaat	cctcctctga	cccccttgca	tatatgaaac	agacagccct
9781	acccctgaat	ctcaacaaaa	cactttactt	atatccttcc	tcccacctgg	aatttttcta
9841	ttctgtcctt	gtcctggctg	atcttagcct	agtcaagagc	tggctgaaaa	cttgccttct
9901	ccaggaaggt	tcacaggtta	tctctaccag	tagggtttgc	tctctggctt	ctctgagcta
9961	ccttatctgt	cttactttat	ttttgatggt	ctttgccacc	ttccttatct	ctgctcactt
10021	aattagattg	gaagtatctt	aaagacagga	actgagagct	atgtgcttgc	atgtacacca
10081	accatgcaca	gtactgggaa	tgtagaagca	tgtgatagat	acattgcttg	actgaactat
10141	catgtcatcc	tcagcaaaact	aatgaaagct	tcadagttga	gaggtgcttg	gaacgttcta
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10261	ggattaggca	tctgaaaata	gatatacctc	aagttcaaat	cctattgagt	tttttcccat
10321	atccttaaaa	aaaggtcact	tcagctcctg	agattttcat	ttctccatgt	gcaaattcat
10381	gtaccctgca	aaggtgccac	agaactgaca	ttctccttct	ctgaacttta	caagaagctc
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10501	tgggtagaaa	tgcccttctt	gtgcttagtg	agaatgccat	caccacatgc	tccaaaagaa
10561	tgctctcaaa	ctcaggattg	tgaagaatc	gctaaggggt	gggaagctgt	gcaattctga
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10681	actagctgat	ctaaagatag	ctcccaacc	tctaaaacaa	gggcatgaat	gagaggggac
10741	ttgtgttgct	cctcagccac	catgtttgaa	tggcagagct	ggacggccca	gttagcagac
10801	tttgtttcat	tcagctgggt	ttgtttctgt	gggaaaactt	ctttcaggca	gctggcatgg
10861	attaccctgg	cagcactaac	ctgcagcaga	ctaattccac	aaaagtcctc	atccctaaca
10921	aaattgcca	aagccctggt	caaggcaaat	gtatgaagat	ctgacatcct	tagtcattct
10981	gtgggtggct	ctgaccttca	aaacatctca	ggaagggcac	attggggaca	aaggtatccc
11041	ttgggaaagt	tatgtccgac	aaacagcttg	aaccctaaaa	catccatcat	gacttcgatg
11101	tggctcagtc	tgatgttcag	gccagtaga	cccaataaat	cccttttcca	gcatctaccc
11161	tgggtgaagac	ttttcagggg	cttattatgc	aaagctgcct	aagcaagaca	gaatttatat
11221	tgaacctggc	catgatttct	gagccgccac	tgggtgttct	gatgacatac	acatctcgag
11281	gttgaagtca	aggagctgcc	aaggacaaga	gactggtggc	aggataaaag	cagtgtgatt
11341	ccttccagta	aataatggtg	gggtggcggg	ggaggtggga	aggggacgct	ccggggagga

FIGURE 3-D

11401	agaggaccgt	agcttttctt	gtaccaaggg	tttgcccttc	aaatggcatc	cagacgtgac
11461	caaataaadc	tctcctctgg	aggctaaaga	atgtgtacaa	tgcaacaaaa	gtgaggtggg
11521	ggagaagcct	gctttatcta	gggtgaatca	tacctagaaa	gaaaacatgc	atccgtcaca
11581	gaaatttcat	tgattgagaa	aatattttta	gtttcctggg	ccacagactg	agtccttcct
11641	gaaactctca	ctatgagctg	ggcactcgga	tggtgcctcc	tgagtgtgat	cgctataga
11701	agcagactat	tgattagaga	aaattcttag	acaaacagat	ccccagccct	catctttgcc
11761	actggaatgc	aaaggggtgct	gccctcccca	gtaaagggaa	tatcgggtctg	gtattttaaca
11821	cggccacaaa	gaacatggtg	ttctatagtc	aattctctat	acagcagccc	aagtgttttt
11881	tttttttttt	tttgaaacaa	ggttttgctc	tggtgccag	gctggattgc	agtggtgcag
11941	tggaggagtg	tagcctccac	ctcccagatt	caagcaatcc	tcccacctca	gcctccagag
12001	tagctgggac	tacagacaca	cgccaccaca	cttggctaata	ttttgtattt	ttttatagag
12061	gcagggtttt	gccatgttgc	ccagcctggg	ctggaaactcc	ggggctcaag	cagtcagccc
12121	gtctcagctc	cccaaagacc	tgggattaca	ggtgtgatecc	actataacca	gccccagtg
12181	tcttttaaaa	acagaaatca	gggtgggcca	cggtggccca	cgctgtaat	ccagcactt
12241	tgggaggctg	aggtgggtgg	gtcacgaggt	caggagtctg	agatcagcct	ggccaacaca
12301	gtgaaatccc	gtctctacta	aaaaatacaaa	aattagccag	gtgtaatggc	ggacacctgc
12361	agtcccagct	acatgggagg	ctgaggcggg	agaatcactt	gaacctggaa	gacagaggtt
12421	gcagtggacc	gagattgcac	cactgcactc	cagcctgggg	gacagagcga	gactccatct
12481	caaagaaaaa	aaaaaagtg	aaatcagccc	atggcattct	ctcctactaa	cacttccaat
12541	gtcttctcac	tgcaactcaga	gcaaaatcca	aactccttcc	catggctaca	ggtccccagg
12601	ctggctgggc	tcacctttcc	tgcttcatcc	tgctccctgc	ctccttcccc	gctgggctcc
12661	atcctcactg	cactcctttc	tgctcctctt	ctataactaag	ggatctctac	ctcaggacct
12721	ttgcatatgc	catctcctct	acctggcattg	acatgcttct	cccagatctt	cttgtagctg
12781	actgctcctc	tgagatgtct	tcttaggttc	accctatctg	gaagtagccc	accctacccc
12841	aacctgccc	taccttttgc	tatctcatat	actttatttt	tttcataaca	ccactatcaa
12901	agtttttctc	tttgctact	gatcatctat	acacaactaa	attgcaagt	ccacgagagc
12961	agcgtccttg	tctcatcaga	ttcccagccc	ccaacgcaag	acttggcaca	taggaaatgc
13021	tcgacacata	tcactcaaca	aaaaaatgaa	agctctaggc	ccacctgcaa	ctgacagctt
13081	gaatgatacc	gaatcctggc	cttgtagaag	gctggaagtc	agtgtctggc	ggagacccc
13141	agcacaggga	ataagaatca	cacagctgcc	accacctgat	tcctggccct	ttctgcccac
13201	cacaacataa	atgacagcag	gtcagtgcca	cagtccacag	tccacactca	aatcttgatc
13261	atggccaccc	acatacccca	aacctggaga	gagactgggg	tgaggtagat	aaacgatgcc
13321	attcaagaca	tcagacattg	ctttctatgc	ccaaaaggca	cattccaggc	ctgtatttgg
13381	caccggaaac	tagcagtgcc	agaagatggg	ctccaacata	cccatcccat	gtccctcaaa
13441	gggcctctct	ctggactaac	ctcttctgca	tggtctttcc	tgacagagctg	atccgtgtcc
13501	tcctgcagag	ccctgggccc	acgggtgggtg	ccaggggcag	cggcaggatg	gggggtgggg
13561	tgcttgacag	gaaatcaatg	ggaactgaag	gtcatccgga	gggcgcagtc	tccccatcac
13621	gcacctgctg	gcatgggatt	tggtgctctg	acctgccttg	ggggcctctg	ccctcctgtc
13681	agagttgggt	aaaatcagcc	tgcaagaagca	aatgtcctgc	acaccaaag	atctccaggc
13741	agcccttcta	agggacatcc	agccaaacaa	agaagcactg	agtctcatit	caccgcgcgc
13801	aaagttgaga	gtcaccccaa	tctctcttgg	cagcctocta	ggaaaactgt	ctcagacctg
13861	ccatttttgg	aggcacatac	ttgtaaatag	aacaaagcca	gactgacca	gaggctgggt
13921	atgtccccc	acttaagtgg	cctgggtggg	gaggaagtaa	aaatacactg	ggaaccaaga
13981	tgactgaaac	tgaaatcttg	agtgcaccct	agaaatgcct	aaatctgccc	tcaacacctc
14041	tacatgccag	gataacgaca	aaggatacca	aaacctctgt	actgcccggg	ggaaatctca
14101	ttttcttctc	atcccaaaaa	atactggggg	gcttggctga	atctagaatc	tgattttcct
14161	tccccacta	tacttatttt	cccaggttcc	cattctccct	tgcttcccag	acctttcccc
14221	tctaccatct	tcctttccaa	ttcgtccacc	tcattcaagag	tcatttatca	tacaggccag
14281	gagcaaagcg	gtcagcctaa	gtctccaatt	caaaagttga	aaatgggcca	ggcacagggg
14341	ctcacgcctg	taatcctaac	actttgggag	gccaaggtgg	gaagactgct	tgagaccagg
14401	agttcaagca	ccctggccaa	cttgggtgaa	aaccgtctct	actaaaacta	caaaaattag
14461	ccaggcttgg	tagcaggtgc	ctgtagttcc	agctacttag	gaggctgagg	caggagaatg
14521	gcttgaaccc	agaaggcgga	ggttgctcag	agctgagatc	gcaccattac	gctccagcct
14581	gggcaacaag	agcaaaacac	cgctcaaaa	aaaaaaaagt	tgaaaatgaa	tatggtatga
14641	aaataaagaa	aaggccaggc	acagcagctc	atgcctggaa	tcccagcact	ttgggaggcc
14701	aaggcaggag	aatcacttga	ggccaggagt	tgaataccag	cctgggcaac	atagttagat
14761	ccccgtctct	acaaaaaaat	aaaaaataaa	aaaatgtttt	aatgaagaag	agacaccctg
14821	gacataattta	cagaaggata	acaggatgct	ggttatagta	gcaatagtgg	catagttaat
14881	atttatttgag	cattttactat	gtgtgccagg	cactgttcta	agcactttac	atgtattatc
14941	cccatacaac	ttgtaattgt	attattccca	tacaactcca	tgattttata	ccccccctct
15001	cacacacccc	actttacaga	ttggcaaaact	gaggcacaga	gagtcttacg	tgatttgcta
15061	aggatctatg	tggccttgtt	aatacattac	agtcttgcca	gaaccttact	cttggccact
15121	gcactgtcag	cctcttaca	gggcgcctac	acccctcac	aatgagtttt	gcctccagaa
15181	ctagaataac	ctgaacactt	cctttcttgg	aggcactaga	acacttccct	tcttggagggt

FIGURE 3-E

15241	ttctatcagc	atcaccaact	tgctagctaa	tcttagctat	ttcttttctt	tgtgcctcag
15301	tatcccaaac	tgccaaatag	cccagaaata	aaccttctta	tcacagagcc	acctctcagt
15361	aactcaaaaa	aagttaatat	ggggcttcct	gaaaatatgc	catcagagaa	atacaaaatg
15421	tcattatgca	gttttagaac	caaatccatc	ccaaatgtga	gcaaggggcg	atggacttga
15481	agaggccctg	tggttctgaa	catcaactaa	ggcagaaaaa	gagaaatgcc	agaaagtcac
15541	aaactaaagg	gtcagattaa	agaatcccag	aatgttagac	actgtctagt	ctgggtgcctg
15601	gttttattgc	aaaggaaatc	aataaccagg	ccagggtgcg	tggtctcacgc	ctgtaatgcc
15661	aacatttttg	gaagccgagg	cgggtggatc	acctgaggtc	aggagtctga	gactagcctg
15721	gccaaacttg	tgaaactcca	tttctactaa	aaatacaaaa	aattagccag	gcatgggtgt
15781	gcatgcctgt	agtcccagct	actcaggagg	ctgaggcagg	agaatcgctt	aaacccggga
15841	agcggagggt	gcagtgcagg	gagattgtgc	cattgcactc	caacctgggc	aacagagcga
15901	gactccacct	aaaaaaaaaa	aagaaaaaga	aaatcaataa	ccacagaggt	gaggtgcagt
15961	cctcgggaca	taccgaggca	gagctgggat	cagatcctca	gtccagactc	ctagttcagg
16021	gattcctcca	tcgtttatgg	caagggtcaa	caaactacag	cccctcggcc	aaacatagcc
16081	caggactaat	ttttgtaaat	aaagttttat	gggaggcaag	ccatgcccac	ccgtttacac
16141	attgtctgtg	gcagcttttg	tgctgaaatg	acagagtcga	gtagttccaa	cagagaccat
16201	gtggcctgca	aagcctaaaa	tatttaccat	ctggaccttt	acagaaaaag	tttgccgact
16261	cctgggtttt	aacataagcc	ttgaataatg	aaaagcctcc	acctcagaaa	tacaaaataa
16321	tagaatagga	aacctaaagg	tcacacagct	taagcagata	gtttttacaat	tatctcagct
16381	tggtacaacc	taataaaaaa	ccataaatac	agttaataat	aaggaaaaaca	agcactagct
16441	cacctacact	atttaataat	tattgttaac	tacagcaagc	aaaactcata	gctgaaaatt
16501	cgtttggttg	cttttttcta	gcctcccttg	aaagccctgt	ttcatctagg	aaatgctgtt
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16741	actccagata	gaacctcag	gaacagccag	gcatggaaga	gactgtcttt	atggcttccct
16801	ctccctactg	ggcctccatg	ccctgcttac	acccctttcc	ttcccagaaa	gtgatcagga
16861	tatgcacacg	gccacacaga	gccagcccca	cagctatgcc	atcattctat	catcccatgg
16921	aatagggaaa	agcgggtctg	cccctgttag	gctgatgtgg	gaatcaagag	acctgatttc
16981	cagattggag	ttggaactta	gtcacttttg	gtttttggca	aatctctcaa	gccctctggg
17041	cccagggtctc	ccacgtcaaa	tgagagagatc	gtcttcacat	attccaaatg	atggaacacg
17101	ggcagagcca	aattaagggg	tggggcaggc	caaccacgtg	gcacccgggc	tccagtctct
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17221	actttgagaa	ataggacctg	gctttcatgg	aatagtccag	ttcgcatcaa	ggtcccactg
17281	taatgattat	tacacttttc	cctctcaaaa	gcgcccttgc	ttggctgata	aatgataaag
17341	tcacctact	aataagctgt	ttgtggtggg	agtgaggtga	gacacgtggc	ccaaggcacg
17401	gcagtaaatg	gcaatacatg	ggcttctaag	gaagacaagt	tcagtttggg	caagaggtgg
17461	ggtgcaggtc	cggggccaga	actgactgctc	taaggacaag	agaggagagg	ctgcctcttg
17521	tgccccggct	tctccatttg	ccatgcacac	agcctttgcc	tcttctttta	tttgtcaaat
17581	atttagagaa	tattcgccaa	agtgtgagct	cccaggagg	cccacaggtg	ctggagagaa
17641	gagagggctt	tgagaggtac	tgtaaggtga	aagaaacctc	ccaacaggtg	cctaactgcc
17701	tgccatgtct	aagcgcctga	gccttgaggc	agggatatgat	cccagccctt	cacagtgcct
17761	gacctgacg	ggcatgcact	tggttaagtgt	tcattctggg	gacctggaac	aagcgagact
17821	caagccctcc	ttctgttctt	ggaaaactcc	tcctccccat	ggcagctgca	tctcgaccac
17881	caatcctact	ggaccacagg	atgcaggagg	actacactgt	gtcctggatc	tcgtcattac
17941	aagagcagga	ggtgagcact	gagaaagatc	cagaagaact	catgcaagca	gaggctgtgg
18001	tctgtgggga	ggaaggccgg	gcagggcagc	ggaccagagg	aagaagcaac	aaagaaggaa
18061	gggggaagagg	aggaggaggga	ggaggggggc	cgcagagtca	ctgtgggtgg	agggagagga
18121	ccgccagcac	atgccccaca	gccatcaata	tctcttcgga	ggacagatta	tctggggaat
18181	ttatgctctc	taataattac	cttcagagg	gttccactta	tcttaccaga	ggaatctgcc
18241	agttgccaga	cacacaggat	tctagtcaat	tccatccaca	ctgccctccc	cctctgcccct
18301	cctccccacc	tccttggtct	ctgacttctg	acctctgaat	tctaaccttt	ctttgcctct
18361	ccagtctagg	gggagggtga	tggtggaagg	gtcacacaaa	cttttaacag	atgtaaaggc
18421	caacaaaggg	gttggtgggt	tgtcccttat	cagtagatat	gagagttaac	gtcccaaagt
18481	tgaggccagg	cctgaggaag	tataggctct	tgccaaagac	agtgtgtgaa	gggccaagca
18541	atgctttggg	gcagactgac	Wtgattat	ttgtcttcac	ctgatgccat	cagacctggt
18601	taggattaat	tttatcttct	agtcttcaca	tcctcctca	aagccttcct	atccccaStc
18661	cagccctcca	gtgaggcctc	cctccaataa	tggtgtgggt	acttatttga	aaaccatcac
18721	gtgttgcttt	gggttgctgt	ggtttcttta	aacgcacgtt	gcagtcctgg	ctgtgagctc
18781	ctggagaaca	tggtgtactgc	atccgtactg	aatcaggact	acctgagcaa	cagtaacaac
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18901	atttcatctc	cacaacaacc	ctatgaaaga	gatgctacta	ctacccctca	ttatacagct
18961	gaggacctgg	gagctcagac	agcttcagtc	acaggcccac	ggtcacttgg	tcagtggcca
19021	agtcaggatt	tgaaccagg	ggtcttgggt	cagagtctgg	gctcttaacc	actccacacc

FIGURE 3-F

19081	acgctgcctc	tgtaggagag	gtttgctgac	tgattcggac	atthttgtgtt	gtatctatcc
19141	gcttatthtaa	gtcatoccttt	tctaaaataa	taathththth	tgagacatgg	tctcgctctg
19201	tcactcaggc	tgtgcaggag	ctctgtcact	caggagtgc	gtggcatggc	tcactgcagc
19261	ctcgatcttc	agagctcaag	caattcacct	acttagctac	cccagtagct	aggactacag
19321	gcatgtgcc	ccattcccag	ctaaththth	ththththth	taagagagat	cggtgtctac
19381	ththththth	aggctgggtct	caaactcctg	gactcaagtg	atccacctgc	ctcagcttcc
19441	caaagtgtcg	ctgggattac	aggcatgagc	ctgggtgcac	ctgggtgtgt	gtcctcctc
19501	cttaggactc	cactcactgc	tccctcctca	gggggcctcc	cccaaactcc	ttagctctgg
19561	cactcattct	ththththth	ctctgtgcaog	atgccaacta	tcaaaaatta	ththththth
19621	taggtgtggg	tggtctatgc	ctgtaatccc	agcactthtg	gaggccaagg	caggcagatt
19681	gcttgagccc	aggagttcaa	gaccagcctg	ggcaacatag	tgagacctct	tccctactta
19741	aaattaatta	attggccagg	cacaatggct	catgcctgta	atcctagcac	ththththth
19801	cgagatggga	ggactgcttg	agaccaggaa	ctcgagacca	gcctgggtcaa	caaagcgaga
19861	ccccatctct	taaaaaataa	taataaataa	aaaaataatta	attaatgtat	atgththth
19921	actacctgct	ththththth	gatataaaag	cttctctggga	gaaagactgg	tctaaththth
19981	tcacccctct	atcaccagtg	cctaagagctg	gtccctagca	tatagtaggc	actatataaa
20041	tatgagttgg	atgaatgaat	tgtctgatgt	ccccactgag	cattccataa	tacatgatgg
20101	ctacttaatt	ggacactthta	ththththth	actcatctat	ctgtththth	ththththth
20161	ththththth	accaggccacc	ttgtctgagta	ggthththth	tcactgtacc	ctgatattag
20221	gtagagaata	ttgtctthth	cattctcatg	ttacagatga	ggaaactgag	actcagaggt
20281	tacacagctt	gccccagacc	atcacagaaat	agggttaagac	ththththth	ththththth
20341	ccccctgagt	ccatgatatt	aagcattctg	cctcattgcc	tctggctggg	tccccctagt
20401	aacatgattc	tctthththth	tgaaactctg	aaatgtcccc	agccttactt	ctccccctc
20461	aagagcccca	tcgcctctth	ctctggcctc	tgtgtgctgg	ctctctctca	ththththth
20521	cagattctct	ctctgccatt	ctthththth	ctgggtgctg	cggaagtctg	tctgtatgg
20581	tcagccattt	gccccctctc	ctctgctcct	gggtgctggt	gtcaatggca	gggtgcccga
20641	gagggaaag	agacagggga	ththththth	ccgccccctc	ctgctgtgga	gtgtctgcat
20701	ctgcccactg	aaggtcacag	ctctgtggtg	ccagccctct	tcatacagct	acctctgcaa
20761	tctgggtgacc	ththththth	ccccgacctc	gccccaggtc	gctgcactag	ccccccacca
20821	tgtgagtcct	tgccccagct	ththththth	gacatgttac	ththththth	tcagththth
20881	tcgtgtggag	ctgctgctth	gctggaaccc	tgctctctcg	acatattgag	gctacatggc
20941	ctctgcccct	ccccaggctc	ccccaccact	gcccgtgccc	cctggctcact	gcagctgcct
21001	caccaggccc	ththththth	ccaggtthth	ththththth	ccaagacctc	ththththth
21061	ththththth	ggcttgaagg	ththththth	cagccccacc	aggagagaca	gtgccccggg
21121	gagcccagca	agcccacagc	aagctgtcct	ccaagacta	ggagaaagca	gagagcatcg
21181	gggtccaatgc	aggggtcccc	tatgtctcgga	gctthththth	gtgccccggg	ththththth
21241	cctcagatga	tgctctggtg	cctcaaaaca	agccgacctc	acagctthth	aatcacataa
21301	tcattththth	agcaactact	atgtggcagg	ththththth	ccattththth	acactctctt
21361	tcattththth	agacgagaaa	aaacaagttca	cagaggttaa	ggaattthth	caaaacctca
21421	aaactactaa	gtggatgaac	tggaattaga	tcccagggtca	gccccaatct	ataaggcctt
21481	aattccccac	cagtacatgc	tgctctcatga	ccgatcccc	tgatgacag	gaggccacca
21541	gactcgaaac	tagtccaggc	aggcagctca	gagatgccag	ccacccatgg	ctgggaggag
21601	atcagggtgga	gcaggatgac	agttaggata	aagggcacag	agggtctcat	gctgcttaga
21661	gtcactthth	ccaaggacca	tgccacagtt	tgcccatagt	gactgctgag	cagccagggg
21721	gctggaacat	gccccccacc	ccccccccca	acccccgacc	actgctcctt	cctgcagagc
21781	cagccaggag	ccatcactcg	ththththth	cacaccagca	ththththth	acaagcctgc
21841	aagcacagac	ccctctgagt	cagggcccag	actgtcacga	ggagactctg	aaggggaggg
21901	gagggacagg	gtgacacaaa	gagggggaag	gctctcctgc	gctggacctg	gagccgactg
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22081	aaagaaaaga	aaagaaaaag	aaatccacat	ththththth	gggagcgatt	cttgagggca
22141	aacacactct	cttgacacac	cacacccac	agcgctthth	ccacacagcc	caaaatagtc
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22261	ctgctggcca	gctctcagtc	ccccgggtaa	caaagtactc	caaggacccg	cagtagcagc
22321	gcctgctcct	acagaccatt	tcacccctcc	cagcgaagtc	ccatctgctg	tgctctcatg
22381	gagccagggtc	cagtttagcag	aggccacttc	caatgaccca	gtgtggccca	aatctccaga
22441	gctgacctga	acctctctcc	ctcaacccct	ccaaatctta	gattgctgct	gctgcttctc
22501	caggggaatg	gtccccacaa	cattththth	actgcaagga	aaatatccag	aactgagacc
22561	gttcttcaaa	ataataatth	aaaaaaaaaa	aacactgctg	aaacacagaa	ctgggtgtta
22621	tcttaaaatc	tctgcacaaa	tagaattthth	atgctctcac	tccaatcaaa	atcattctcc
22681	gtccctccct	ththththth	aaagttcaat	tccccctaaa	gacaggattg	caaacatgat
22741	taggtccaat	taattththth	agaaactcag	aatgaaagga	gagaaatcaa	tagaactgcc
22801	ththththth	cactaccgca	aatgaagtga	ththththth	gagatctgga	aagaaaggaa
22861	accaaagtg	tcacaccgca	gccattggcc	ththththth	gcagcattgc	cccatgtgga

FIGURE 3-G

22921	ctggctgggt	ggagaagacc	actcaagcct	acaagacact	cctggggaca	gagggagggg
22981	agagacagct	gaggtcactt	gctttctctt	cattgtacag	catgaggctc	actggtggta
23041	aattctcctc	tttctcaca	aagcaagacg	taaaagaaag	taaaaggcaa	aaagcatcca
23101	cacaagctgc	cagtctaata	aggacactgg	taatctccag	gcaggccaag	gccatattggg
23161	ctccccctgc	agcttcatgc	taagttttatc	tccatcctca	cactctacct	ccatctctct
23221	tccatatcca	ggaaggaaaa	aaggaaatta	acaagccggc	atccaacatc	catcctgaat
23281	caccagctgg	gccatgtaga	gcatccaaag	atgggggtggg	gaagccccag	gggagagaga
23341	gacattgaca	gatcaccgtc	cccacctctc	acttgcctgc	agctcccttg	catagatgat
23401	gctggcaaat	tcaacgtgat	tttctattgga	cctgcccagc	agtcacagatg	tgggagccta
23461	ataacaaata	acaatgccag	ctccatgtga	tccttgcacc	ttcaagagaa	aatgccttgc
23521	tggccagctg	ggttctctgg	ccaccctcca	gccaccttg	ctgcttcttg	atggagggttc
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23941	ccaccaccag	tgccagaaaa	agccagctca	tgagttaact	cccaggcagt	attatccact
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24361	caaattacta	caaaacttgt	agtttatgaa	aacacaaatg	tacgatttta	cggttctaga
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24661	ataagccagg	ataatctcct	caYctcaaag	tccttaactt	aatcacacct	gcaaaatccc
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24961	atatataagg	cagatggtgc	ctaagagcat	aggatttggg	accacatcgc	tctgggttca
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26521	ggttttagaga	aaaggaggaa	ggagagtgtg	caggtcttcc	caatggggta	aggcgaggca
26581	tgaggaaagt	acaagaaatg	ccaagccagt	aagaagacag	gacgaagcat	cgcacctgga
26641	tagaagacta	agtaaaacta	ccttctgtgt	gctaaggggt	ctactaggat	acactcattg
26701	acttgctttg	gccaacagaa	tacagtggaa	gtagatttac	accagttcca	agctcaggcc

FIGURE 3-H

26761	tcaagaggcc	ttgcaagctt	cccttctgct	ctccgggaac	cctgcctagt	tgcttagcat
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26881	cctagatgaa	gctattcadc	taggacaagc	tgactgcaga	cacataggtt	aaccagccca
26941	aatcagaaga	accagctagc	tgagcccaaa	tcgaattgcc	gaccacgga	atagtaaagca
27001	aaataaatgg	ttgctatattg	aagccattaa	gctttatgg	gttttggtat	gctgcaaaac
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27121	ctggcatgta	atagttacac	agtaaacgct	tcatgaataa	agtattgaac	tgatatatca
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27961	tactttttga	tggttttctag	tggtttttata	atatactctc	ttaagagccc	catttatcct
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28321	ctttccagag	acttctgccc	agtatgggaa	gtcagaagct	ccacactcca	agtatggctc
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30481	agttatgtag	ttgcaagttg	aacctacaca	caaataggca	tgatacaact	aaagaattaa
30541	aacggcagcc	cactgcagtc	agggggccat	ctgacaatat	aggaaaggag	ataactatag

FIGURE 3-I

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31381 aatgggtgcc tggacaaggc tttcatctca tggatatgc tgtcctgaac acaaggcaca
31441 agacacaaca cgggaggacc tttcatctca tgtctcttac agccaggggac tgaagggtga
31501 ggacagtagg agaaaataga gtttcacata aaacacccca aggacatcaa agaaggctag
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31681 ccatggaaaa caaattcctg ctgagtagca aagagagtgg caccaacaag tggcaccatg
31741 tgagtgaaca gagcaagcaa atgctcacac agggacagct ggggtgtgcag ggccatcaca
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32341 atatacacia agggaatata tttgtatatt ttcagatata aagtggatgg gaagcaaggc
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34261 tgtttgtgtt tttgtttttt ttcccaataa ggaggcagaa agtagaggag gtcgtgagca
34321 cgagaaagtg ccactgctag ggtatgacac atagagccct caaaggtagt tgaatctgat
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FIGURE 3-J

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FIGURE 3-K

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FIGURE 3-L

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45001 atagaataac tacgactctt acacactgcg tgtgggaatg ctaactggta cagccacttt
45061 ggaaagcagt ttggcaattt cttttaaagt taaatataca attatatattt catttctccc
45121 agagatttgc tcaaaagaaa taaaacata tgtctacaca aagacctata aataggaata
45181 ttcatagcag ctttctgcat aatggccaaa acttgggaac acccaagtgc tcatcagttg
45241 gtaaatgaat aagcaagtgt ccatgcagcc acacagtgga acgcacccat acatgcagta
45301 acatggataa gctttaaacc catggtatca gttcctattg ctactctaac ctactctac
45361 aaactcagta gcttaaaaca acacagattt actgtcttac agttctggag gtcagaacgt
45421 ccgaaatcag tctcactggg ccagcatcaa ggtcagtttc cttatctttt tcagctccta
45481 gaagccacct gcattccttg acccatggcc ccttccctca aaggcagttg tgttgcatct
45541 tctatctaac tgcttaaggg aacaggactt tatcaaggca cagagccaca gcaagtatgg
45601 gaaacatata agtagttcca tatttccagg gtgtgtaatg taacatttcg aagataagga
45661 aactgagatt cagagagatc caatatctta cccaagggtc aggacacagt gaaaatcatg
45721 ttcaacccta aggcctctga atccaaatcc agagtccacg tgagccctca gacttccctg
45781 ccttgaccgt ggatagtcac ctccaccttg tctcagagcc ctgcaactcc accctgttac
45841 actgcaccag cagctaagcc tgtggagcca ggcagaacct tgggcctccc cacctcccca
45901 ccctgggacc aacagattcc cagctccagc aggataacat cataacctta ataagattga

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FIGURE 3-M

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45961 catttgcac cgtgttttata ttcatcagca ttcttacact tacgttatgt tatctggcct
46021 tctccatcgt atgagctctaa tgggtgcagat attctccacc ccacattctc caaccctcag
46081 aaagctgagg tacttttctta tacagcaagt gggtagaagc caagatcaga accttaccce
46141 caaccacccc cttgatacca gaagagccta ttgactcaga acaaaactca ggcaaacccc
46201 ccacctagct gagcttcccc tcttctcatc gcaggatgga aaacagggta atacctgccc
46261 tgcctatcct gatacatcag gcataaatgg aaaaaaaaaa aaggaagtag tatgtaaaag
46321 cactttggaa atgttaaaat gctatgcaaa ttataaggaa ctgttctgat tatactctca
46381 agaaatgtca caaattttct ccaaaagtga ataattgtca ttacttttca acttcatccc
46441 cttgaaaaagc cagtttctcc tctgtcatc ttttatttct ggttaaagca gagatgttat
46501 actcaacatt ccaactggaa tatcaagatc aatctttaat tctccttcc agcttcccc
46561 tttctgaaat caagaacagg caattctcta ctccaccac catctcatcc tcagttctc
46621 ttgccatctg cccccctctg aagctagaaa tcaccagcaa ccattttcat tctcatccc
46681 tcYggtctct cctcagtcag agccaaccta catgatgcaa aagcaccact ccaatcacct
46741 ctctcagagg ctccagccc cggggggaca gcgtccagg gtcctccacg ggctgcccc
46801 gtgaagctct ccagcttgct tccatgact caccaaccca ggtaagccta aatggccctg
46861 tttcccaaaa ctcaactctc ttcccacttt tatgtcccca ctatatctgg aactcccttt
46921 cccactattt aattagctat ggggtagga agaatcaaac tagaccccca gctcttacct
46981 caacctaaat atattccaag tgaatcaaag aattgtggtt aatggctggg cagggtggct
47041 cacacctgta atcccagcac ttaagaggc caaggtgggt ggatcacctg aggtcagagg
47101 ttcgagacca gcctggctgg gtaacatggc aaaaccccg tctcaactaaa aaataataat
47161 aataatacaa aaattagcca ggcattggtg cgcaagccgg tagtcccagc tacttaggag
47221 gccaaaggcag gagaattgct tgaacccacc cagcagatgg atgtttcagt gagccaagat
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47341 acacacacaa agaattgagg ttaaaaaaaa tccagattat atagatgaat atctatctga
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47461 aaatgaataa tagttaacat ttacctattt tcaactcttt taactggata tocatatttt
47521 aaaagtaaac atacccttta ctctatgttg tacacaaaaa ataacaaaat ggatcacaga
47581 atgaaagaaa tgctaaaatt agaaaaatc cagaagaagg ccaagcacgg tggcctgtaa
47641 tcccagcact ttgggaggcc aaggtgggca gatcacttga ggtcacgggt ttgaaaccag
47701 cctggccaac atggtgaaac ccctattaaa aatacaaaaa ttagctgggc atgggtggtac
47761 acacatgtaa tcccagctat tcaaatggct gaggcacaag aatcccttga acccaggagt
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48361 aagataggag atatggtgtg acaacaatgg gagtataatt cacaccacta aatactcaac
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48781 taaaactaca gtaagctacc gttcacaccc attaaaatgg ctaaaattca aaagactggg
48841 aatgtcacct gctggtgaga atatatagca accaaaagca cagccactgc tgacgggaat
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49501 cacttgagcc caggaggcaa aggttgcagt gagctgagat tgcaccacta cactccaacc
49561 tgggcgacaa agtgagaact tgccttatta aaaaacaaaa ggtagatagt gtatgattgt
49621 gtttacatga actcttagaa tcagcaaaaa taatctacag ttacagagag ggggtgagta
49681 caaagaggca ctaaggaact tttggggata ataataatat tctattgtgg ttacatgggt
49741 atacacattt gttaaaattc atagaactat ataYttttaa tgagtacatt ttattgaatg

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FIGURE 3-N

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49921 taaaaagcat taagacctca acaggcaa at ggccaaaaga cacagaaaag ccacaaaaga
49981 ggaaataaga atatctaata aacagggttaa aattaaagca atgaaatact gtatttcaca
50041 aaccaaatga gcaaatttca cctatcaa at gagttttttt gtttttgttt tttgctttga
50101 tgataatttt tgttttgttt ttacttta at gataatacta gtattgtagg acaagatgag
50161 cactcttctg gtaaaaatat aaattgatac atttctagaa cacaatttgg aacactatta
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50281 ttgaccctct tctagaaacc tgtgctaagg aataaacaaa gatgaatgat caaaattaga
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50581 gaccagcctg gacaacatga tgaaacccca tctctaccaa aaatacaaaa attagccgag
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53461 ttcacttatg ggacaggcac ccagtggcaa tcattgtgag aaatagggag aggcgatctc
53521 atgcttaggg agctcagaaa atgctatgct tccctccagc tgtaggggag ctgagccact
53581 ggggaagagt ggatgcattt ggacaaacag gaatggatgg aaggctttct agggaggggg

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FIGURE 3-O

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53641 accacatgag caaagcctga agaaggggtg gttcttatct agcaatgag agagtgtgag
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55261 gatggaaagt cacaccctca agaaggcccc tggggaagac agattgtctg ggatgtggat
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57061 tgtgcaatat tctggccacc tgggtttttt tacttgggat accaactcct agtactcaac
57121 aaccattccc tttactcttt tttttttttt tttttttttt tttttgagac agagtctcac
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57361 tcaggtgatc tgcctgcctc agcctcccaa agtgcctggg ttacaggtgt gagccactgc
57421 gcctggcccc cctttactct taaatacagt gtgtgccagc tgtagtagtt tatgcctgta

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FIGURE 3-P

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57481 ctccgagcat ctcaggaggc tgaggcagga ggatcacttg agcccaagag ctttaggctg
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57601 ttaaaaaaaaa atacaatgtg taatggtgat ataataattc aaaggttaat catctctact
57661 tttgaaaaaca ataatgaata ccttgctttg cttttgttta gcctcacatt tttttcagag
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58801 tgccaggctt tccttgtttt ccactttata catgtgcact ttttgtccta tggagattat
58861 taagatcatt agggcaaaat tccttttgac ctcccataag gcctctcaca gtacaagaca
58921 atatgtggtc aataaatatt ttttattaaa tcaaaactca ggagcccaaa gaaccatca
58981 ccaggcattg ccttacttac aacatgagat atttgccttc tttaatccct aataaacagt
59041 tttttgtttt tgagacagag tcttgctctg ttgccaggc tggagtgcag tggcacggtc
59101 tcggctcact gcaacctctg cctcccaggt tcaagtgatt ctctgcctc agcctcccaa
59161 gtactggga ttacagtggt ccaccaccac gccagctaa ttttttgtat ttttagtaga
59221 gacaggtttt caccatgttg gccaagctgg tctcaaaact ctgacctgtg gatctgcctg
59281 cctcagcctc ccaaagtgtc gggattacag acgtgagcca ctgcatctgg ccaacagtat
59341 tttttattta attcctagat aaagtaattc ctgatgctt gaatttcaca atccaagata
59401 attttttttt gagacagagt ctgctctctg caccaggtt ggagtgcagt gccgtgatct
59461 ctgctcattg caacctcacc tccagggttc aagtgtattc cctgcctcag cctcccaagt
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59581 gatggggttt caccatgttg accaggctgg tttcaaaact ctgatctcaa gtgatccgcc
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59701 caagatattt ctaacaacaa caacaaaatt ggagcggttca atgtggtctt gccaaactttt
59761 gttttaacac cattgtttct taaagaaaag aacattgaat acatatcccc aaagtcaagg
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59881 taacactgga ctgaagaatt ctttgctatg gcagtggagg ggaaggagaa gggggagctg
59941 tgggcaaaat tgcaccagtt cagaaccact gaatttttta aagtaogctt tcttaaaaaat
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60361 actgctaccc aaattttcaga ctttctgggt caaaaggacc ttacacataa tatagtggac
60421 tttcaataaaa cacttaccaa atggacaaat gaaccccttg tcacccgat ctactagtt
60481 ccttccctga aacccgacac atctgagtcc ttttctcctt tactaacctt ttctccaatc
60541 ctgctcatgg gaattaaagc tgtaaaataa gcctggcgca cctcgggccc ctgcccctgg
60601 ctctgtgggt gggagcactg tggaaagcgt atcaatcgcc cccacctatg agagcctttc
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60721 cttggatatt taacctggag gcggggcaggt gacagaaaaa ggaggtggca agatccttga
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60841 ggcacctcaa ggaaacgtga cgcgggaggg gattccgagc ctctctgtct gcttacttga
60901 cagcaagcag gtcagagttc ctgccatttc cttctagtag aaacccacc aagaccacct
60961 ccccgccctt gcaggcaaa gactggtagc tctcccaagg gaaaaaaa acaaaaaaca
61021 cacactcctt gttacaaacc agacacagtc ctggacagag cccagctaac aataaatttc
61081 tggggttcat ctcaaaagta cattaagtat cttctgacaa tctcccaaag ggctgggttt
61141 ttctggccat cacagggctg tagaatattg agtacaagga gagggcttca agaacagggg
61201 atccaagccc tcgtttcatt gatggggaaa ctgaggctca gagaggggga aggaacttgt
61261 tcaggatcat ccaagtatgc tcccgctcagt Rgcagcactg agccaagaac tcaaggcttc

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FIGURE 3-Q

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61321 agttttggca ctgggttttg ccagaggett gaaaacatac caagaagtgg aaggtgtact
61381 atgagctaaa tctcactttt cctgaaaaata tagatgtgtg ctcacacaggy cacacatgtg
61441 cataaaaggt agggaaagag gaaaacaaat gtagcaaaat gctagtaaata ggtgaatcta
61501 agcaaagggg atattggtgt tcattgctct attttcacaa cttttcagaa ggcttgccat
61561 ttttccaaga aaaatctgag gaagggctag gtgtggtggc tcatgcctgt aatcccagca
61621 ctttgggaag ccaaggtggg aggatcgctt gaggtcaaga atttgagacc agcctgggca
61681 acataacaag acccatctc aacaaaaaaa ttaaaaattg ccaggcatgg tggctcacac
61741 ctgtagtccc agctactcag taggctgaag caggaggatc gcttgagccc aggagtccga
61801 ggctgcaatg agctatgatt gcactactgc actctagcct gggcaacaga gtaagaccat
61861 gtttctttta aaaaaattaa aattaaaaaa taaaaaattt tgaggagaa agataaagca
61921 ctaactagca atctaagata aaaaattttt taaaaaaaat cacttggaaa agagttagaa
61981 ttctccttcc aatttcattc agtttcccta gctagggact aatatcctta gaaaaagtta
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62101 tagcagtccg cagctacagc aatcttagaa tccaaatagc atttcagata tttgtccca
62161 tcagctccta aaatacatat attctgttca caccatgtat cctctgttgt ttttgggtgca
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63001 aggcgaaggt ttggcagagg aacgttggtga gttttgaacg tgttgaggtc ctggttgat
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64981 ctggaattac aggcattgag ccaccatgcc aggccaggat ttctttgtag ggtgatgaaa
65041 atgttccggc atcagatgtg gatgatggcg gatgtactaa ccaccactga attacgcact
65101 ttcaaatggt tagaatggtg aattttatgt tgtgtgaatt ttctctcaac agaaaaattc

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FIGURE 3-R

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68881 ttaaatggca agcggaaca aaatcgtatt cccattttct gaatgagaaa acaagccta
68941 aaaggaggac tccaagtaa tatcaacttg caaacctatg aattttttatc ttaataactg

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FIGURE 3-S

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69001 gctttgaggg acctttggca acagcaaagg cattcggcaa tttgtgtgga agtcacatta
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69121 ggcaggcagg cgtggaagtg agatccacgt gaaagaccta agcaotgact ccccagggga
69181 ctggcgaaat gacgcagggg ccagatagat gtcagatttg gccaaagtgt cctcctttct
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70561 ttagaagaga gacctctgct tcctagaaat acaaattccc aggcattggg ctggcttcca
70621 aactctagct cctccagttc ttactgcac aagtcatttc tgcaagttc cattttccca
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72421 ccagcacttt gggaggccga ggcaggcgga tcacgaggtc aggagtttaa gaccagcctg
72481 gccaacatgg cgaaccctg tctctactaa aatatataaa aattagccag gcgtgggtgc
72541 agacgcttgt tatcccagct actcaggagg ctgaggcaag agaatacatt gaaccagga
72601 ggcagaggtt gcagtgagcc gagatcatac cactgcactc caaccgggt gacagtgtga
72661 gactccatct caaaaaata aataaataaa taacatgat taaggataaa gcaatccagY
72721 ggacaaggct cttggagcca tattttatgt gKcatgtatc attccgggga gctctcctct
72781 gtcaatgcca agactagcta gtcagtggtg gagaaaaggc attctgtgag aacagatgaa

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FIGURE 3-T

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72841 aggggaacaga gaaactggca ctttcttttg aaaagagttg tttccaaaac ctagatgtgc
72901 agcctctacc ccaggttaatt agtccaacac actatccatt acagctgagt ccgggtttgc
72961 ttcaaaagca tcgggggttt tttgggtttt gcttccctta aaaaaaaact tgttttgaat
73021 gaggggaaaa aggcgtagtt aatttttata cagaaatctg ttaaagagat ctgatcaatg
73081 gtgacaaaaat ggaagccaga gatggaaaaag attcactgtg aggctctggc actgaaggcc
73141 aacttgggct tccattcagt tcaataataa tatttatcat agctgctaac aatttttttc
73201 tcttttttga gatggagttt cactctgggt gccagggtg gactgcaatg gcgtgacctc
73261 ggctcactgc aacctccacc tcccaggttc aagtgattct ccggcctcag cctcctgagt
73321 agctgggatt acaggcatgt gccaccatgc ccagctaatt tttatttttt agtagagatg
73381 gggttttctcc atgttgggtca ggctgggtctc aaactcccaa cctcagggtga tccaccgcgc
73441 tcagcctccc aaagtgtctg gattacaggc gtgagccacc acaccagcc aatagctgct
73501 aagacttacg caggtttaca tatgttaggc attgctctct gagcttatat atattaactc
73561 attccatctc tatctatgag gttgggattg atataatccc cactttacac ccagagaggg
73621 taataaactg cccaaagtca cacagctaatt aagtgacaaa gctaggcagt ttggctagag
73681 tctgtgctct taacaattat accatatgtt tcctagtaa gcatttctta tgccgtact
73741 atgtgctggg caccatgctg gacaaaagga gtactgagat atataaaaca cgggtacaca
73801 cataacaggt tctagtccat gcaatgatga gaatcatata ggcatctctga ggtctaattt
73861 cagaacaaaa cgtagaaaaa ctgcctccac acatctggac attagacta aaatgcagtg
73921 cctgttttct cattgggtatt attctattca atagagtcaa ttttaagact aagcattcct
73981 tgacacccca cccatccttg ggtcatgaaa ctcaataaag ctctcttcat tttgattgga
74041 ggggggaaaa tccccgtaa atatgtttgc ttctttttcc tgaatcacc tctgtgtga
74101 aaaggattgc ttaccactga tctaacaggg tcttgaatac agggtccttc agagggtaca
74161 agaagcccag gtgttcaggt tattaaaaaa tgaagaaatg caaagcagga ttacaacatt
74221 tttggcacat tatagatcct cacacaacaa atttacattt tcacacacac tcacgcacaa
74281 acacacatac aaagtcacaa acacaatgta aaataattat gatcacaga ggatgatagg
74341 ctctacattt ttaaattattg actcagaatg ccctgggaat gacgtggtca aggcacagac
74401 tgtgcatttg acactttgtg atgaacatct tgggtcacat ataactagt gcacagataa
74461 tgtcaaagtc tcattagaat cctccatgga accaggtatg gtggctcata cctgtaaatc
74521 ccagtatgtt gggagggtcaa ggcagagcga tcacaaccag gagttcaaga ccagcctggg
74581 caacatagtg agtccctgac tctacaacaa atttaaaaat tagccaggcg tgggtggcacc
74641 cgtctgtagt ttcagctact tgaggatcac ttgagcccag gaattggagg ctgcagttag
74701 ctataatcgt gccactgcac tccagcctgg gtgacagaga aagaccttgt ctctaaaaag
74761 aagcctccag gaatgggaaa cccaagttaa atcagctccc actccaccct aactccctc
74821 ctaagccttc ctttaaggaa aaagaacaaa atactgagcc cagtagtaag gaaagaacag
74881 tgaaagcccc agttaggaaa ccatgaaaga gaagaaatga ggtacacagg gagaaaacgt
74941 ggatgaaaac ctagactat ggccaccaac agacccaagc tagccagggt tagacctctg
75001 tgacacctag aggtcaagtc caagagggtca gctgaagtta cgaaaggcag gcaggaactc
75061 aatcagctac ctacttgttc acgagctagc cctcccagg cctggcatct atgcttacct
75121 cctggcccac tctgtctggc ctctccacag gcacaggtga ggccctaaac accaggatc
75181 ttctaattgtg tgctgccttc tcccacgtct gtcccatttc ctaggagtta atcatggtgc
75241 ccattgcaac atggcaccca atgccacttt ccagagtagt gtgacgtcca attccaagac
75301 ctggaggata aaaggtatta aagctcctgg gaccacagaa gagacagggc agaaagctgg
75361 tggaaaacca tctccaacat ctgtttcttt ttctgttaaa atctatccac tgtgtgaatt
75421 gccaaaggaa gtttaagattc ctgtctgtaa acgagaagggt ttctcttttc acatgaacc
75481 tgcagaagat gggaaacatg atacccctcg cagatcagag gacaccggct cctgtgaaga
75541 ggatacccca acccttgtca gtgcagcacc cggcaggcg atttttacat ttttctcctc
75601 ttgctgaagg gcctccagaa aggccaccag ggctttcccc aagagtaaaa ttctccccag
75661 ctccctagga ggtctcactg cccaccaccc ctttattttag ctaagtagca gagtttttat
75721 tttactgttt attttatttt attttatttt attttatttt attttatttt attttatttt
75781 agacagtctc cttctgtcac ccaggccgga atacaatggc atgatctcag ctactgcaa
75841 cctctacctc ctgtgctega gcaattctca tgtctcagcc tcccagtag ctgggattac
75901 aggcacgtgc caccacaccc agctaatttt tatattttta gtagagatgg ggtttcacca
75961 tgttggccag gctagtcttt tttttttttt tttttttttt ttgagacgga gtctcactct
76021 gtcgcccagg ctggagtcca gtgggtcgat ctoggtcac tgcaagctcc gcctcctggg
76081 ttcacgccat tctcctgcca cagcctttgg agtagctggg actacaggcg cccgccacca
76141 cgcccggcta atttttttgt attttttagta gagacgaggt ttcacatgt tagccaggat
76201 ggtctcaatc tcctgacctt gtgatctgcc cacctcgcc tcccaaagt ctgggattac
76261 aggcgtgagc caccacgccc agcttaggat agtcttgaac tcttggcctc gagtaactg
76321 cctgacctag cctcccaaag tctgggatt atgagccact gcaccagcc agtagcagag
76381 tttttaaata acttcagag ccctttactg gagacacacc caagaagatg ggctcttatt
76441 cttccacag aggactatag accatcaact aaattcactg gctcctactc aagctataga
76501 aagctgagga ggaccttga acatcctctc taaattcctc ccctagttcc agtccaggta
76561 aacaaaaatt gattctattt tttcaaaaca ccagcccctt cagatggcct ggtaactctt
76621 cattaacatg ttatcttcat taacatgttt atcttcatta acatatctt cagtgtataag

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FIGURE 3-U

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76681 aagggcccag ggttcaacat cccactttgc atccatgcag acaagggctg tgggaagctg
76741 taaaactgaa gaggcggtga atccaggagg gattccccag atatccgtga gttgggtgtt
76801 gactttcttg aacacgtctt tcctttactt tacacttaca cttactgagc attcactctg
76861 gaccagaccg cgtcctaaga gcttcacgtg tgtggtcatt caatcctcaa accaatccta
76921 tggggtaggt actggagtta agtgaatggc ctgggatttt aaccagaag tctgattgca
76981 aagcccaact taccatgagg gccacgacat atgtctctac ttacggattc caccagtact
77041 cttgacagga gcatttacct cactatatta taagccttga tctacttttc tatctccctg
77101 aagcataatc agccataatc tgctaaccgt gcctcagttt tcattctcct ttctattttt
77161 tttcagcgg gggcagggga gacagaatct tgcctgttca ccaggctgg agtgacgtgg
77221 ctcaatctgg gctcactaca acctccgcct ccagggttta agtgattctc ccacctcagc
77281 ctcccagagta gctgggatta caggcacgta ccacctgccc cagctaattt ttgtattttt
77341 agtagagacg ggctttcacc atgttgggcca agctagtctt aaactcctga cctcagggtg
77401 tccacccgcc tcagcctccc aaagtgtctg gattaaaggt gtgagccacc gccagcctc
77461 attctccttt ctttattttt atgatagcct ctaccttgag ttccacccaa gcctatggcc
77521 atctgctcca aactacattt cccaacatcc cttgtggcca ggtgtggcca tgggcctaag
77581 ctaagccaat gggatatgag tgggaagctcc ttaatgacaa gctacttgcc ttgtgatttc
77641 acctcctgct tctcacatcc tgaaatacag acttaaggat acaaaataga ctaaaacctg
77701 ggtccatgaa tgatgacttt ctggacctac cttacctgcc tgggtgtgctc gccaaacgac
77761 ttatttgaca aataaataaa cttctgtcct atttagcttt ttaattttt ttattttttt
77821 tttggacaca gagtctcgct ctgtcgccca ggtggagtgc caagtgaat ggcgcgatct
77881 cggctcactg caacctctgc ctctgggtt caagcgattc tcctgcctca gcttcccaag
77941 tagctgggat tacaagcatg caccaccatg ccgggctaatt ttttgtattt ttaagtagag
78001 acagggtttc actatgttgc ccaggctggc ctcaaattcc tggcttcattg tgatccgccc
78061 gccttggcct cccaaagtgc tgagattata ggcattgagcc actgtacctg gactattgta
78121 gccattctat ttggggacct ctttgttata gcagcttagc ctgtatgctg gattcagcac
78181 ctgaagtccc acagcttgtc ttattctatt caacatctcc agaacccttt cttagggtct
78241 ggaacatagt agttgctcag taaatatttt ttagctgaat gaaaacacca ttatgtaaag
78301 caggtagtac cagggtcaaa caaactgatt tactcaagct gtgcagggtg ccggtatcca
78361 ggtgactaca atgtttcctg ctttcttggg aaacaggagt tcaggacaga gtagtaggtt
78421 ttaggaaagc atttgcaata ggaaaggggt aagctttcac tgcattctgt gttggctctc
78481 tgctgagaca acagattttg ggcttaatca aaagttagct gaggttactt cttgtctgat
78541 aaaaataatg ggctccattt gagcacttac tgtgtgccag gttctgtact aagcgcttca
78601 catacattat ggcattcatt ttcattcaat tctcacaata accctacaag gtgaaaaata
78661 ttaatatctc cagatgaaca aaccaggccc ccaaaaaagt taaataactt gccctagctg
78721 catggctcgt tagtgacaaa agtaaaattc aaacccaagt tgtttgagcc taaacttact
78781 ctcttcataa ccaatctgcc actctgcttc tcttctctgt tgacaagcca atattcccca
78841 ctatggttat aagtttcaag ggtggacca cgttttgtgc ttatctcaat agacgccaca
78901 ggcacggagc ttccactggg ggtgtgaca cttctctctc gtgcattgatt ggtgaggggt
78961 tgcacacacc caccaggaga catgacggca gagggcaaac actctgagac ccagggtcca
79021 cccagctctc ttttgccctc tcctctccct gggctgcccc ggctgcctcc ttgacctctg
79081 cactcttctg cccacgctgc tgccgcccac atcttggaac gcatcccccg gggccgctt
79141 cctgcctgtc ttttgttaca attcctgcca ggcggggcag ttctcctagc taaagccggc
79201 aaggtccaga cctgcccgtc tggcctggta atgggtgtgt ccacatttca cctccacct
79261 tcacctcaac ttcactctca tggccattct ttatccacaa caactccttc ctcccattc
79321 cctagactca gcaaagcagt caggagctag gcaaggtggc ctttatccca gagggtggga
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79441 tggttgtgca ctatgctttt tgaaaactga gttagctagg tttaggtggg gcacagtggc
79501 tcatgcctgt aatctcagca atttgggagg ccaacctggg tggatcacct gaggtcagga
79561 gttcaagacc agcctgacca acatggtgaa accacatctt tacttaaaaa atacaaaatt
79621 agccaggcat ggtgtcatat gcctgtaatc ccagctcctt gggaggctga ggctgaagaa
79681 tgccttgaaac ccaggaggtg gaggttgacg tgagccgaga tcataccact gcactcctgc
79741 ctaggcgaca gagagaaact ccatctaaaa aaaaaattag ctagggttaa agtcattaga
79801 ggtcatataa aaatgcaaat tcaaaacttc tctcagaaaa tcaggagccg tgacaaact
79861 gggctcacct ccccatgtgg caaatggctt ggggtgaatg tgaacatcct ccctggaagg
79921 gcataaactt cccagttgac cacagtacag tcccccaacc cccacctccc accaactccc
79981 tattcttctg ctctacaggg ttacatggc ctgactagcc cccagaggca ttggagtttg
80041 acacgcccac agcagtgcct ccattttgccc gatgagcaaa ctgagaaaaa gcaaagagaa
80101 attagtcccc cagatctcca agtgagttcca cagggctggc aatcattaga aatcattaga
80161 caatatttat ccagctccca gatgtccccc cccctgctct gttcagtcac tgcactcatc
80221 catgtggctg ccccaatgcc ttgggcatgc cagagagaca cctcattctt tcaacacaca
80281 ggtcacaaac atcttttgtg ccatgacaat ctgattctcc tcacgtcacc ccaagattaa
80341 ctcttttcaa atctgtggtt cagattatac accctgaagc tgctgagggg tgacctctca
80401 ataaggctaa tctcccctgg acctaaatac tgggtggggc tgtgtgcatg tgtgcatgtg
80461 tgtgtgtgtg cgcacgcgca tgtgtgtacc catgtgaact cgctcatgca tgtgcttcta

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FIGURE 3-V

80521	gattaacact	ctttcttctc	attaacttcc	cagacagggtg	agaagtcaac	atttgcccca
80581	gttagagaac	cagaaagtat	cagtcctcact	gccccatcta	aaggggcagc	agctgctgat
80641	ggttgccata	gtggaatgaa	gattcagggt	tgccagatct	ttcaactttt	caagaagcca
80701	ggaatataac	ttagaagagg	ggagcaatgg	tctctaaaga	cctgtgctga	gaaacaagtt
80761	cctaagtgtc	tgggagaatt	tatgaggacc	aggtgctaga	gaatgccggg	aatgaacgc
80821	tcccccttga	acgtcccat	ggtgagggtca	gaactatgtc	ctcaatccct	catcagccta
80881	tcccaggact	ctgaagagga	ccccagggtg	cttggctggc	tttgcttcc	agcctaagaa
80941	tgtctttgac	taatattttt	cttaatccct	gtttgctctg	tcctcaaaac	aagccttttt
81001	ctctttttct	tatccatctt	ctccatagag	ccctcagggt	cttaactcac	acggcactat
81061	ctggatcttt	ccagtaagta	ggttgctgtt	tccatttctt	tgattaaaca	actctaaca
81121	agaattcatt	gagatgaaaa	tgcttatcat	gaagcaggta	acatcctttt	cctcccaaaa
81181	ccacaagcaa	ttacatata	aatggcctgg	caaagggact	tctttgagag	gtggcagatt
81241	ataactactc	ttgctcctac	acggataaag	ctttttttta	aagacaggaa	agaacaattt
81301	acaaatgaga	aaatgtcaca	gatggccaca	aactaacttc	ccgagggatg	agtattttga
81361	tgcagatact	tottcaagtg	aaaaatgtac	aatgtacaaa	atgtccactc	gaggatctgt
81421	tcctccccgt	gtgggtaatc	gccctcctac	cacgggcaac	gggtaggcaa	ccgatatgcc
81481	cagaaaggcg	gccaatggga	ggacagctcg	cccagcctcc	cgattggcca	ggccccccac
81541	cagctggaac	catggcgagc	tttgaggaca	gcagagccac	ttgatgggat	tctctctctc
81601	ttcaaagcat	agagcaaaac	tcaattaatc	ctcaaaagac	gctttcaaga	agaacattat
81661	cccttttggg	gacgcagaag	ctaagagggtg	ccgcaggtag	gtgaagggaa	ggcagggaagt
81721	tgaagaggag	aggagaaaagt	ggagcaccgg	gctttcagcc	ccagttcttg	ttctctctag
81781	agagtcaagt	tgcaggagaa	gaatgaacct	gcagaagccg	ggcaggggaga	gggtggtggag
81841	aagccgctgc	tcttgggtgc	gccctcaag	gcttccact	gccccatccc	ctaggagacc
81901	acggagtga	aaaagttgga	ggcctaagta	cagccgtgtg	taccagccg	ggcaggagag
81961	ttaagacaac	tggacttgtg	ctcaaaaacc	cttctttagt	aaaacaaccc	gtaggagtct
82021	gtgggaggag	gaaaaattga	agtctggatg	caatttgcca	caactgagtct	gttctggtaa
82081	ccgcccccaa	cacactcaca	ccccttggc	tgaaatgggg	agaggggtg	gatcgggtgtg
82141	tgtaaacaga	ggcactgccc	tgcttggtg	ctctttccat	cttagggaga	ccaatccaga
82201	actttctacg	gctcacactc	tgatcacagc	ctgtcgccat	gattggcaat	aaacgtcaca
82261	cattctcacg	ttatacattt	attcgacctt	taatatgtgtg	ctctgagatt	cctggaaaac
82321	ttgtatgtca	ttggtcaaac	gttataaaaa	cagccacta	ttttttcccc	actcacatcg
82381	tccgtgttga	ctgccttaca	caccgatttc	tacatggaat	gttttttagcc	tgcattttaa
82441	cacttagaat	aactttcttt	gccacacact	acatacatat	tgtttgcatc	aataaacaga
82501	gcccgtgcca	catgcaagtt	ataggtttat	tggagacatt	taagtgttta	tagaaaggac
82561	ttttctaaag	aatctgaatg	ggagtctctt	caatttacca	atagtcaaag	aaataaagaa
82621	aattacccta	cagctgattt	ttttttaatt	aaactaccaa	caactattct	gccatagcct
82681	tgcgtgtgtg	tgtgtgtatg	tgtgtgtgtg	tgtatgcatg	cttgctgagg	catagaaaat
82741	atctggaagg	atttacaaaa	actccttagc	tttggggaac	agaatggaca	gacagagaga
82801	aaacctcttt	ttttcttgtt	ttatgttctt	tactgtgcat	tgtttacaat	gagcatgttg
82861	ttgttttttt	ttttaagact	agtcaagagc	agcagtgaga	aagggggaag	gaaagaacaa
82921	ggagttcaat	ctgtaactgt	gaacaatcaa	ttgagataac	tcactaccct	cagactagcc
82981	accatgttgc	tttttaaatg	tttcaaatca	caaaatgaaa	aagttactct	aagatcatct
83041	attttttccc	cagggtgtgt	attttgtccc	catgcctgtg	caaagtaagc	cagttagaatt
83101	tagaaatagc	ttgctgcctt	tttttttttt	tttttttttt	tgagatagaa	gcttgcctta
83161	ttaaccaggc	tgcagtgcat	tggcacgcat	ttggctcaac	acaacctctg	cctcccagat
83221	tcaagtgaat	ctcctgcctc	agcctcccaa	gtagctggta	ctacaggcgc	ggaccaccat
83281	gcctggctaa	tttttagtag	agacggggtt	tcactatgtt	ggccaggatg	gtctcaaaact
83341	cctgaccttg	tgatctgcct	gccttaggct	cccaaagacc	tgggattaca	ggcatgagcc
83401	accatgcccg	gcctgctacc	ttttttacat	acacaaaata	attgcaaact	ttcactgcag
83461	tactgccaac	cctcatgtca	ccatctacaa	tgtaccacgt	caagaaagga	caatatcttc
83521	aaacccactt	accagaagaa	aaggttgaag	ctgtatttgg	caggatactg	acatacaaac
83581	ctccaagatc	tgggaaacaa	ctcaggctcc	ttgacttgac	ttccttaacg	atgacttgag
83641	aaacaccaga	aagtccagaa	cacataaact	catgaaacca	accaatagac	tggaatctct
83701	ctgtttatta	aagtcatctt	tttggccagg	cgcagtgcc	cacacctgta	atcccagcac
83761	tttggggagg	caagatgggc	ggatcacttg	gggtcaggag	ttcgagacca	gcctggccaa
83821	catggtgaaa	ccctgtctct	actaaaaata	caaaaattag	ccaggcaagg	tagtgcattg
83881	tatagtccca	gctactcttg	aggctgaggc	aggagaattg	cttgaacccg	ggaggtggag
83941	gttcagtgta	gccgagatca	cactctactc	tctctactct	actccagcct	gggtgataga
84001	gtgaaatcct	gtgtcaaaaa	aaaagaaaaa	acaaatcatc	ttttattctc	ttaaagaatg
84061	aatttttcat	gggccatcaa	cttcttcagt	catttaagta	tttgtttaga	gaatatattca
84121	gttagaaact	caggaaatgg	agacctgacc	tcaaagggcc	ctttccagtc	ataaagtaat
84181	tagaaataaa	ataaaaacag	gttgaagtga	taagctgata	agaaaatcca	atttgtttcc
84241	aaaattgttc	acttacagct	gtttttctca	tgaatatagc	tatagtgtgc	atcagcaaat
84301	cagtggcctt	gaattcgaaa	ggagtgaaaa	tatacatcct	gggtctcttg	aactcctagt

FIGURE 3-W

84361	gtttgccaga	gctaggcagc	aggatcaaat	ggtcaatttc	agcctggccc	tgaaatcaaa
84421	accctctaac	agtcacagaa	gttctgcagc	tagtcagtta	cttactgccc	acacttcact
84481	cagcacaatc	cttaaagtca	ccagaggag	cccaaatttg	cgacaaacca	gaatgctttc
84541	cttttagggc	atagttgtcc	ttctgattct	acttttgccc	tctcctttcc	aagactaatt
84601	tagaaacgaa	gggaagtagg	ctaagaaaat	cctcaccttt	aatattaata	agacttgtgc
84661	agtccccgga	tgatcagagc	ccagactaca	taggacttga	aagaaagaat	gagactttga
84721	tatggaatat	gaaaaagtaa	caggtaggag	gggtggagag	accaaactga	gaggcctagg
84781	gcccgacttc	tgcagctctg	tcactgactg	gcccgggtgac	gatcacgcct	atttactaag
84841	cagggatgac	ctacgcttac	ctgtctacat	ttttatctgt	gagatgaacg	aatgaaacc
84901	tccaatgggt	tatttgccat	gacaattttt	aaaaatcagt	aggaatgagg	gaattaggaa
84961	ttgagcccat	gctatacctt	cttttcaaaa	gagatttcac	atgtaccatc	tcatctgtat
85021	tcttgagag	atagtagccc	attatgagtg	gctccaattt	acagaaaaag	taactaaggc
85081	acagagtggg	gatctaccca	ggacagcatg	gtctgtagaa	gaagcattgg	tctgtttagt
85141	gcattgaaat	gtattccaga	gatattggtc	tgtaaagacc	ttcccagaat	gtgtctagaa
85201	ggttcaacca	cctggtggaa	gacatagaac	gccttgtcat	gccttcccc	ttccagcctg
85261	gagttctctc	catggtctca	gcctgcttct	atgaagctta	gttttatagg	gagcctttta
85321	accaagccaa	cctcagagtc	ccactggcca	aggggatggg	gggggaggca	aaggattcta
85381	ctggggcagt	atgtaaccca	catataagtt	ccatccaaag	caacgcttcc	aaacctagct
85441	caccaggaca	ggagaaagg	taccatcagg	gtactcttag	ctgagaactc	atacctttcg
85501	ggctttYatt	ggcttgaggc	atgagtgtac	agcagagccc	cacatcacia	tccctgtact
85561	cagatataaa	ttatattagt	gggcaggga	tgtcaggaaa	cttaggttgt	agaatctaga
85621	tcaacaactg	cttaccgagg	agctgggtga	attgtaaaga	aagaaagaaa	caagtgttga
85681	atgactgtgg	cctcattaaa	catcttctgt	gcttggcctg	tgctttgggc	tttcccagag
85741	ctgtttcatg	caatagcttt	gggcaggcca	cttcttttga	cttactccaa	ctacacaagg
85801	aggaggagga	tgtctatggg	tctttccacc	ccagacacag	tatcagtcac	agccccacct
85861	taattccact	actccaattc	tgttctgagg	gtatcacagg	atgctgtggg	gggttcccc
85921	gccccacaaa	atccttttct	cctctaaaa	aggagaacat	ctttccttcc	tttctgatca
85981	tccatcttgc	agccagcagg	actcccagcc	agaacattgt	caatttactc	agggatccat
86041	gaggcacctt	ttggaagatg	agaggggttg	gggtaaaaa	ggaagaggaa	gtgggggtgct
86101	ggtacttctg	gaaacaagcc	atttctcagc	ctgctctgtg	aagggtcccc	aaaccttaca
86161	cagatctagg	aagggaaact	gcattccaag	aatgcatggg	ggctagaagg	accgctgga
86221	gcattggatcc	caccacaggg	agataatatt	ttgaaaagag	cacacattta	accagggaag
86281	aagagcccat	gcccctggct	aagagcatag	ctgtttcctc	ctccatctgc	ccccattttc
86341	ccaggcctga	ctagagcaag	tagttaagcc	aacccaaatc	cagaagtatg	aataatgcgt
86401	gaagcacagg	aggacaggca	gatggccttt	tcacctgcgc	aggctatata	gctctgtgcg
86461	gaggggctga	gagtcacagc	cgccccctgt	gccccctcag	aactgtgcaa	gaggaagtgg
86521	gcctcccctg	cgggggtatg	aaatgtgggg	cgaggactta	ggagttcacc	gggaagtggc
86581	agccatctcg	gggcagacac	caagagctgg	agtgtattgt	ttaccctttt	tcatgtagtt
86641	aatttgcttc	cagcagattc	cattagtgtg	ctgacagacc	aagggcctgg	aggagggtcc
86701	tggaagagct	gctgaatcag	cagactaaag	gggcgaccag	gaaggccaga	cgtctgtcac
86761	cgagcccttt	gctcagagtt	tctattttga	gagcttagaa	taactatttg	ctaagctcct
86821	gtcaaggcag	cacctctaaa	ccatgtatgg	agagaagaca	cacaaacctt	gaccacaaaa
86881	tgtgaatggc	caatcagaag	ctgacacaa	cagctgctga	ctgaggaaaa	atgattttat
86941	gggggaaaag	aattcccaaa	tgaaataata	agcaaaagtt	ataaaacttat	taaaaagcct
87001	gttaaaaact	tacttaaaaa	gcaaaagttt	aaacatgggt	ccatctgcaa	ctaggaactg
87061	gtcggggagg	gagggtttga	acttcctttg	agtttcaatt	gataatcccc	gaagattaa
87121	aaaatagtga	tactattact	actgctgctg	ctattattac	aaataataat	aactacaatt
87181	aacattttatt	tggcacctag	tacatgctag	gaagtaggca	atgagttttt	ttgtttgttt
87241	gtttgtttgt	ttttgagatg	gagtcctact	ctgtcaccag	gttgaggtgc	aggggcgcaa
87301	tctcggctca	ctgcaacctc	cgcctcctgg	gttcaagcaa	ttctcctgcc	tcagcctccc
87361	gagcagctgg	gactacaggc	acacgccacc	atgccagct	aatttttttg	tatttttagt
87421	agagacggcg	tttcaccatg	ttggccagga	tggtctcaat	ctcttgacc	tgtgatccgc
87481	ccacctcagc	ctctcaaagt	gctgggatta	caggcgtgag	ccaccacgcc	tggcctgcaa
87541	ggagttcgtt	atgcatgatt	tcatttactc	cttgcaacat	ctctttgagg	tagggaaaact
87601	gtgtgggtga	gaaaagtcac	atagctgtca	agtcatagaa	aacgttcaga	gcaaaatcaa
87661	acccaggtgt	aggccagggt	cagtggtctc	tgcctgtaat	cccaggactt	tgggaggctc
87721	aggcaggcgg	attacttgag	gccaggagtt	caagactagc	ctgggcaaca	tggcgaaacc
87781	ccatctctac	caaaaatatg	aaacaaatta	gccaggatat	gtggcataca	gtgtgtgtcc
87841	catctactca	ggaggctaag	gtgggacgat	tgcttgagcc	tgggaggcgg	aggttgagct
87901	gagccaatat	cacaccactg	cactccagcc	tgggtgacag	agttaagact	ctatctcaaa
87961	aaaaaaaaaa	aaaacccagg	tgtgtccaac	tccaggcttg	tgcacttacc	cactctgcta
88021	tatggctaaa	tcccacaggc	tacagagaga	gcagggaagt	aggactcagg	agaactgcct
88081	ccagccccc	aggcaccctg	actagctgtg	ggatcttagc	aagtgttttc	aactgtggg
88141	ccatcgtatt	ccatcagatg	attgatgtct	tagggacccc	ttcaattcaa	accacagtta

FIGURE 3-X

```

88201   ttggtggact gcctgagtgc caggcactaa gataggggggt gggggaatgt ataaacaaaa
88261   ctaaggcgtg gtccttccct ccaggagttt acagtctagc cctgccttat gcaaaagcca
88321   aagagcctta ggtgtccctt cagggtctaaa atactactca gagattcctt ttgaacatgc
88381   aaagtatttc tgacagcatt catattcatc ttctatttgt tctgtgtgga catttgcattg
88441   gagaggatc tgaaattatg ttcgtccaat ggatttgggg tgataatttt gctctcatct
88501   ttttactttt atgtgttgct tgaattttta gtaacaaata tacatcattt ctataaaaaac
88561   aaaggcattt ttaaaatact gctaaataac actatatatg ggtgtatatg tataatgtata
88621   tatgcacaca catacctata tacacatata tatttaaaca gtaactggat atttaataat
88681   actgtggaat tattgttaac tcagataaga ttgtgactag gtttccagaa agaattcttta
88741   ttttttgcag atacatactg aaataattta cagataaaat gatgtctgag atttatttca
88801   aagtaatctc tagtgtgaga gggtaggagt aggctataga tgagacaacg ctggctctga
88861   gttgcaagtt gtggaagcaa tttgggtgct aggtgatggg tataagagtg ttcacgatac
88921   tacataggtt tgaaattttc catactatac agtaaaaaag gaactccttt caaggccaac
88981   agggaagcaa catttcccca aagctaagct aagcacccag ctggcagcat ttctacctgg
89041   ggtttctacc acccttggct tcctctcttc tttgactatc tatcacagtt taacttcatt
89101   ggttctctgc agcttccctc ccccccccc ccacaccatt cccccctaac cttctggaat
89161   cacgtgttgt atctatttgt acattccagt gcccaggcca tccctcttctg acctaccctt
89221   ggcccagggg acagagcggg tgggcctgag caatgctccc acacacctcc gctcaaagtc
89281   agctgtttgc tgtagaggta gaacagcttg actactgggg gcgagggtca cagttcactc
89341   attccccag caaatacgga gccagatgct ggggactcag cagtgaacaa gaccaaattg
89401   ctaccttcac agagttttca tgctagagaa ggagccaact ataaatgtta tctcccatcc
89461   ctcccagatt tagggccagg ggtatattca ccaagacatt cctgaatcac ctgggatctt
89521   gtcccaaata atttaaacct gaaagacatg atctagtgcc aagagctaga ataccacca
89581   actaccatc ccaatccagt tccccattta actgacaaaa aaaaaaaaaa acagaaatgg
89641   tgtaagccca ccatgtaagt aaacataagt aaacagtggc agaggaaagg gtaccagac
89701   ttcactgtgg caggcccacc tgggaccaca ttcagaattt ttacaagctt Wgctgcgatg
89761   ttgaccaaag ttctccccac tttttttcat ttgcttgaat ttcactttta tttttattaa
89821   catcttttgt tttgttttgt tttgtttttg agacagggtc tcaccctggt gcccaggcta
89881   gaatgcagtg gcacaatcat

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FIGURE 4-A

>4:68275001-68368000

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1      caaagaaata aaagtaaaaa aaaaattaaa aatgactcaa taaaagagaa atcacaaatag
61     aaaattataa agtataaaaa aagagccatc acacttcatt cttcctaagt cctacaccag
121    agttgtcttta aatgtgtgta tttaatgggt aaataagacc tgaaaaggga gttggcctaa
181    aaatatttttt accgtRaaac atcaattttct tcagagttaa tgagaattat atgctaacca
241    taccaaaaaac cttgattaga attttttagct tagatgtatt gattgatatt aaaaaggga
301    agttgaggcc acatacagaa agcaattggcg aaggacactg cctccaacag aaaatatgaa
361    ccaaaaagca taatggaaaa acattttacat gtaatatact aaatagatgt catgccaaaca
421    cagacacaca aggtgagaat accatgtgat aatgcaagta gattgaaatg ctaccggtgc
481    aagccaagga atgccagaaa ttgccagtaa accaccagaa gttaggaata aggaaggatt
541    ctctccctta cagggttttca aagacatcac ggcccttgaca acaccttgat ttcagacttc
601    tagcctctag aactgagata ataaatttct gttgctttaa gtcactcatt ttgtgttatt
661    ttgttacagc agttctagga aattaatata aacatgcctt ttaccacagt tctctcccat
721    tggattatttt aataataaat gatttaaaat tagtatttgg aaaagatgtt ttttaatgag
781    tagacatatt aatcagggtct cttttgacac agaaatgttc tatatttcat tttcatattc
841    ttgtcaaatt ataaaaataa tatcataaat atggacatcg ctacaagcta ttatgtacag
901    tcaactgaaaa atcagaaaaa acatgtgagt tagaaatgtt tatcaaatac aagcttacag
961    aaaactgaat aaaattttta ttttaaaaca tcacaagtaa ttacaaagac aaatattcca
1021   actatacaaaa ctgttttttca catatacata tatacataca tatattttaag gttggttgat
1081   ctttcatcttt tttatctgag taaaaagaag aacactttcc tcattccgga gatttttgat
1141   gttataaatag ttacctaaaa gtaaagtgat aagaaaataa aaattattta catatgaatc
1201   attcttttttg attaatgtat tagtcatcac ctgacagttg tagtatagga cacaagataa
1261   aaacaatttca cctaacctaa agtaacttat ttaattccat gaactacatc aacagctaac
1321   catgacacgt gatccagatg aggcttgaga gaacagaaat ataaatttca catcgttatg
1381   aaaataaata cggagatgaa tcagtcgaga gtgtaagaaa agaaaatctc tttctgaaac
1441   caatctttat taggtctaca gaactgctgt ggattcctct aaccagacat actcatatat
1501   agatgaatat aaaaggtaca atgttaagta gaataaaaac tcaaaatttt attttttac
1561   ttatttttttg tttttgtttt ttctttttct ggagaacggg gtctcgctat attgccagg
1621   cagggtctcga actcctgggc tcaagctatc ctcccgcctc ttgcctccct gagagctggg
1681   attacaggca tgagccaccg cgcccgcca aaatctcaa attttaaaaa ggcaaatgct
1741   actcttaaat aaatgaggta acaataaaca gcaaaagtga aatacagatg gaccgaagt
1801   atcacatgtg acaggcttat tagaattgag tactatcact gtgactttct atattataga
1861   aattgagaaa gtattcacaa cagtgtgac atactaagga ttatgcaagt atggctatta
1921   ttattgtctc ctccaacag aatgtaagct ctataaaagc agggattttt gcctgttttt
1981   tcatttatat atcccaaatc ttgcagcaat acatggacat agtagacact ttgttttgtt
2041   tttgtttttg agacagagtc ttgctctgtc acccaggctg gagtgcagta gtacaatcac
2101   agctcaacgc aactttgaac tcctgtgcctc atgcagtcct cctgtcccag cctcccgaga
2161   gctaggacta taggtgtgta tcaccgtgcc tgggttaactt ttgcattttt tgtagacaca
2221   gggctcttct aggttgccca ggctggtccc gaactcctca cctcaagccc tctcagcct
2281   ctcaaaatgt tgggattaca ggtgtgagcc actgcacctg gcccatagta gtctcttaat
2341   catacttgtt gaatgagtga atgaatgaca agtggaataa aatgcctatt tacaataact
2401   tctgtctgtt gatagctgat gaagcatacc attcttgaaa cagtttaaaa taatgttcta
2461   aaaacataat ttcttagaga taacatgggg taaataattt ttgttctcct ctgtaatata
2521   acatatctgc tgactatata cataaatgta tttttttttt tgagaccgag tctcactctg
2581   tcccctaggc tggagtgcag tgggtgcagtc tctggtcact gcaagctcca cctcccaggt
2641   tcatgccatt ctctgcctc agcctccaga gtagctggga ccacaggtgt ccgccaccac
2701   gccagctaa tttttttgta ttttttagtag agatggggtt tcaactgtgt agccaggatg
2761   gtctcgatct cctgtccttg tgatttgccc actttggcct cctaaagtgc tggattataca
2821   ggcagagcc accatgccc gccaatattt tcatattcag tagtaacaa ctctgtttct
2881   catgtatcaa aacactaatt ggttgggcac tgtggctcac acctgtaatc atagcacttt
2941   ggaggccaag gtgggcagat cacttgaggt caggatgatct gttacggcta acatagcaaa
3001   atcccgctc tactaaaaat acaaaaagta gccgatgtg gtgggtcgtg cctgtagtcc
3061   cagctactcg agagtctgag gcacaagaat cgcttgaacc caggaggtgg aggctacagt
3121   gagctgagat cgtgccactg cactccagcc tgggtgacag agcaagactc tgtctcaaaa
3181   acaaaaaaaa accaccacaa aatgctaata cacttaccta atgatcaaat gaaaggaaa
3241   tatgtaccaa actgttctga catccatcag tcatatcaca cttcattttg accactgtg
3301   cttccatttc catagtgcc aaaaacaact atatacatgt tgtctaagt aataaaattg
3361   tcttacctga aggaacatag aacgaatccc cagtacttaa tatataaggt gtttcatgta
3421   aagtacacaa aaggtcacca aagttaacat aaaaaacctg taaaaataaa aataaaaaatc
3481   tcattcaaaa ctgaacctg ataatacttc aaaggaacct taaaatgtag tgggaagaat
3541   aacgactccc cacaatatgt ctggctttta tctccagAAC ttgtaaatatc attaaatttc
3601   atggcaaaag ggaccttgag atggggagat tatctttgat aatgtaggta ggccaatct
3661   aatcacatta agcccttaaa aatagagtac tttctcctgc tggaaagcaga gaagaaacga

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FIGURE 4-B

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3721 aagagaagga acagtcacag aaatttgaag catgaaaggg acttgcaccg ttgctggcac
3781 taaagatgtg gggccatatg ccaagaaaca tgagttatth ctaaaatcta agaatgacac
3841 cctggccaac agccagttag gaaatgggaa cctcagtcce acaaccactt aaaactgagt
3901 tctgccaaca gtctgaacga gactggaagc agactggaag cagattcgct cttacagcct
3961 ccagaaagaa atacaaacct gtcaacatct tgattccagt cttgtaatac tctaaagaga
4021 atacctggtc aagctcatgg ttctctctac ataactgtga gatagataat acaagagtat
4081 tgtttcttgt tttttgagat ggagtctcac tctgtcatcc aggtctggagt acagtgaggc
4141 gatctcggtc cactgcaagc tccgcctcca gggttcatgc cattctccag cctcagcctc
4201 ctgagtagct gggactacag cgcgccgcca tcgcgcctgg ctaatttttt tttgtatttt
4261 tagtagagac ggggtttcac catggctctg atctcctgac ctggtgatct gccgcctcg
4321 gcctcccaaa gtgctgggat tacaggtgtg agccaccgag cccagcccaa gagtattaag
4381 ccattaaatt tgtgatacag tcatgcaact cctaacgatg ttccagtcaa cagcaaaactg
4441 cctacatgat agtggctcta taaggttaca atggcattta aaaaatcgta ttgcctagtg
4501 acctcacagc catcatgatg tcccagtga aagcattact cacatgtttg tggtagtgct
4561 gatgtaataa aatctactga actgccagtc acataaaagt atagcacata caggaaaaag
4621 tggaggatag aaagtaggac taacttgtag ctccactca gatggacaga acagcatgtg
4681 gaaactcaca tcatgaactt ttttgccaga agaactactg caggaacata ccaagaaaaac
4741 tgaaagaatt cacagactct ttgaaagaaa tggcttgctg ctgcaaactc catgagacag
4801 ctgaacaacc gtgagtgccc aaagtgtgaa aggggggaaa gtctgcctcc aaacacatcc
4861 ttactgggga agctgaaaaat ccaggtcatg agagaaggat ttaaccttac ctgagactga
4921 aacgaattga gagagccaag ggaaatataa tagtagaagc agaggcagga agagccctgt
4981 taagtactcc tggtttccaa ggaaacccaa ggaagccatt tctgacttta tctcataggg
5041 ttccttgggg atggctgcca gtggaactgg gggaggacca cagaaagaag gaaacttcca
5101 gctgaacttt aaataatttt gatgaagcgt gaattttcct gggcagaatt gggggaaggg
5161 cgaataggaa gttcagatac aagccagggt aggcagcaag gggcagggcc tgaaagccca
5221 gcttgctttc tcagcaggga gacttatagc ctacgcgcaa atgtcagtcg tgctacttgg
5281 ctgtctggat acaaacttgg tttggtgggg cacagtagga gtgagactgg cctagcctgg
5341 ctgcttggga gctgggtgag gccagtctct cagcttcccc cacttccttg gtgaccagta
5401 tgatgcacta gagacagcca taatccccct ggaacataa ctccagtggc ctgggaacca
5461 tattttcatc ccctacagtg gtcacaaaaa gctcagccca aggagagtct gagctcagac
5521 acacctaatc aatcctacct gcacctgatg gtctttctct aactgccttg tagcctaaga
5581 caggagctat aaggcccccac ccataccctg agaaacctga atacttacct aggcaacctg
5641 tggcaacctt gtatcagcag atgtctctct gaaagtacca tctcctgggt ggtggccagc
5701 cacctgctag cacaaccaat attaaagaaa accagcacac taaacaaaaa tacaacccaa
5761 gaccgtcaca gagtctgctt cactccccct ctacctccac tggagcagct gctgagatcc
5821 atggctgaga gacctgaaga cagatcatat cacaagacgc tttgcaggca cttcccagta
5881 ccagcctgga gccccatagc tctgctgggt agctagacac agaagagcaa tagcaatcac
5941 tgcagactgc ctctcaggaa gcataatccc taggggaagg aggagagcac cacatcaagg
6001 gatcactcca tggaaacaaat gaacttgaa cgcagtgtct gacctccaga tgtctcctct
6061 gacacagtct acccaaatga gaagaaacca gaaaaacaat tctggtaatg tgataaagca
6121 aggttcttta acacccccaa aagatcatac tcgctcccta gcaatagatc caaacaataa
6181 aatctctgaa ttgccagaaa aataattcag aaggttgatt attacattac tcaaggaggc
6241 accagagaaa gatgaaaacc aacttaagaa attttttttt aaaaatacac gattttgatg
6301 aaaaaatctc gagagaaata gatagcataa ataaaaaaca atcacaactt ccagaaatga
6361 aaggcatact tagagaaatg caaaatacat tagaaagttt taacaataga atcgaacgag
6421 tagaagaact tcagagctca aaaacaaggc ttttgaatta acccaatcaa agacaaagag
6481 aaaataaatt aaaaaaaaaa atgaacaaag ccttgaagaa gtttgggatt atgttaaacc
6541 accacacata agaataattg gtgttcttga ggaagaagag aaatctaaaa gtttggaaaa
6601 atttgaggaa ataactcaagg ataacttccc tggccttgct agcaatctag acatccaaat
6661 acaagaagtt caaagagcac ctggaaaatt catcgcaaaa agatcatcac ctagccacac
6721 agtcattagg ttatctaaag tcaagacaaa gcaaagaatc ttaagagctg tgaggccaaa
6781 gcatcaggca acctatttaa aaaaaaccta tcagattaac agcagatttc tcagcagaaa
6841 ccctacaagc tagatgggac tgaggtccta tctttatcct ccttaataaa aacaattatc
6901 agccaagaat tttagtatcc agcaaaacta agcttcataa atgaaagaaa gataaagtct
6961 ttttcagaca aacaaatggc gagagaaatc cccactaaca agccagcact acaacaactg
7021 ctaaaaggag ttctaaatct tgaacaaaaa actcaaaata tatcaaaata gaacctcctt
7081 aaaggataaa tctcccaggg tctataaaac acacacacac acacacacac acacacacac
7141 acacacccaa agtattcagg caacaactag cacaatgaac agaacagtag ctcacatctc
7201 aatactaaca ttgaatataa atgacttcaa tgctccactt aaaagataca gaacggcaga
7261 atgcataagc attcaccaac aaagtacctg ctgtcctcaa aagactcact taacacataa
7321 ggattcacat aagcttaggg taaagaagta gtaaaagata ttocatgcaa atgggatacca
7381 aaagagagca ggagtagcta ttcttatatc agacaaaaca gactttaaag caacagcagt
7441 taaaaagaca aagaaggcca ttatgtaata agaaatggac tagtccaaca ggaaaaatc
7501 acaatcctaa atatatatgc acctaacacc agagctccca aatttataag acaattacta

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FIGURE 4-C

7561	ctaggcctaa	gaaacgagat	agacggcaac	acacttatac	tcaaggtctt	caatacccca
7621	ctgacagcag	taaacagggtc	atcaagacag	aaagtcaaca	aagaaacaat	ggattttaaac
7681	tatacactgg	aacaaatgga	cttaatagat	atttacagaa	catttctaccc	aaaaactgca
7741	gaatatacat	tctattcatc	agctcatgga	acattttcca	agatagactg	tatgagaggc
7801	cacaaatcaa	gtctcaataa	atttaagaaa	accaaaatta	tatcaagttac	tctctcagac
7861	cacagtcgaa	taaaattgga	agtcaactcc	aaaatgaacc	ctcaaaaacca	agcaaataga
7921	tggaaattaa	ataatctcct	cctgaatgat	tggtgggtca	acaatgaaat	aaagatgaaa
7981	attgaaaaat	tctttgaact	gaacaataat	agtgcacaaa	tctatcaaaa	cctctaagat
8041	acagcaaaag	cagtgcctaac	aggaaagtta	atagcattaa	atgcctccat	caaaaagtct
8101	gaaagaacac	aaatacacaa	tctaagggtca	cacctcaagg	agctagagaa	ataaaaacaa
8161	acaaaaccta	aaccagcag	atgaagatca	ggccatttgg	tagaactaaa	tgaaaatata
8221	atcagaattg	atagaccatt	agtgaaggta	acaaagaaga	cagaagatcc	aaataaactg
8281	aattagaaac	aaaaatgggag	atattacaac	caataccaca	gaaagacaaa	agatcattca
8341	aggctcgtat	gaacaccttt	atgtatacaa	accagaccta	gatgagacag	ataaattcct
8401	ggaaatatac	aactccctag	atataaccag	gaagaaatag	aaactctgaa	aagaccaata
8461	acaagcaatg	agattgaaac	ggtaataaaa	gaattgtcaa	caacaaaaaa	agtccaggcc
8521	gggtatagtg	gctgatgcct	gtaatcccaa	cactttggga	ggctgaggca	ggtggattgc
8581	ctggggtcag	gagttcaaaa	ccaggtcggc	caacatggca	aaaccccgtc	tctactaaaa
8641	atacaaaatt	agccagaatt	ggtggcgcgt	gcctgtaatc	ccagctactt	gggaggctga
8701	ggcaggagaa	tcacttgaac	ctgggagatg	gaggttacag	tgagctgaaa	tcgcaccatt
8761	gcactccagc	ctgggcaaca	agagcaaaac	cccgtctcaa	aaaggaagaa	aagaaaagaa
8821	aaaaaaaaat	tccaggacca	gatggattca	cagctgaatt	ctatcagaca	ttcaatttat
8881	ctatcagaaa	agagacaaat	tcttggaat	acacaacctt	cttagattaa	accaagaaga
8941	aatagaaact	ctaaatagac	caataataag	cagcaagatt	gaaaaggtaa	taaaagaatt
9001	gtcaacaaca	acaaaaaagt	ccaggaccag	atggattcac	agctgaattc	tatcagacat
9061	tcaaagaaga	attggtacca	atccaactga	aatgattcca	aaagacagag	aggagtcaat
9121	acgcaagtca	ataaatgtga	aataccacat	aaacagaatt	aaaaccaaaa	aatcacatga
9181	tcagctcaat	agatgcagaa	aaagcatttg	ccaaaatccg	gcattgcttt	atgattaaaa
9241	ccctcagcaa	aatcggcata	gaaggagcat	aactcaaggt	aataaaaagc	atttatgact
9301	aacctacagc	cagcatcata	ctgaaacagg	aaaagttgaa	aagtttctcc	tgagaactga
9361	aagaggacaa	ggatgccac	tttcaccact	tctattcaac	atagtactgg	aagtcctggc
9421	cagagcaatc	ggacaaaagga	aagaataaaa	gggtatccaa	actagaaaag	aggaagtcaa
9481	actggtgctg	tttgccaatg	atatgatcat	atagctagaa	aaccctagac	tcattccaaaa
9541	agttcctaga	tctgataagt	gaattcagta	aactttcagg	atacaaaatc	aacgtacaca
9601	aatcaatagc	tctgctatac	accagcagcg	accaagctga	gaaacaaatc	aagaactcaa
9661	ctcctttttac	aatagccaca	aataataata	ataatttgga	atatacctaa	ccaaagagat
9721	gagaaatcat	agacgacata	aacaaatgaa	aacacatccc	atgctcatgg	atgggtagaa
9781	ccagtattgt	gaaaatgaca	tactgccaaa	agcaatctac	aaattcaatg	caattcccat
9841	caaaaatacta	tcattcattct	tcaaaagaact	agaaaaagca	atcctaaaat	tcattatgga
9901	acaaaaaaag	ggcctgcata	gccaaaaggga	agactaagca	aaaagaacaa	atctggaggc
9961	atcacattac	ctgacttcaa	actatactat	aaacatatag	ttacaaaaac	agcacagtac
10021	tgaaatgaac	ataggcacat	agaccatgga	actgaataga	gcctagaagt	aaagccaaat
10081	acttacagcc	aactgatctt	aacaaaagca	aacaaaaaca	ctaagtaggg	aagggaacac
10141	ctattcaaca	aatggtgctg	ggataaacag	taaggcacaa	gtagaaaaat	aaaactggat
10201	cctcatctgc	caccttatac	caaaatcaac	tcaagatgga	tcaaagactt	gaaactaaga
10261	cctgaagcca	tgaaaattct	aaaagataac	atcagaaaaa	cccttccaga	cattggctta
10321	ggcaaagact	tcatgaccaa	gaatccaaaa	gcaaacacaa	caaaaaacaa	atagatggga
10381	cctaatttaa	ctaaaaagct	tctgcacagc	caaagaaata	attggcagag	taaacaggca
10441	acggcagagt	aaacagacaa	cccagagtga	aagaaaatat	tcacaaactg	tctgtgcaac
10501	aatggaataa	tatccagaat	ctacatggaa	ctcaaacaaa	tcagcaagat	aaaaccaaac
10561	aatctcatca	aaaagtgggc	taaggacatg	aatagacaat	tctcaaaaga	agatatacaa
10621	atggccaaga	agcacacaaa	aaaaatgctc	aacaataact	aatgataagg	aaaatgcaaa
10681	tcgaaaccac	aatgagatac	cacctcattc	ctgcaagaat	ggccataatc	aacaaatagt
10741	agatgttggc	ctagatgcag	tgaaaaggga	acaattttac	actaatgggtg	ggaatgtaaa
10801	ctagtacagc	cgctacagaa	aaccttagta	gagctaaaag	tagatctacc	atgtgatcca
10861	gcaatcccac	tactgggtac	ctactcagaa	gaaaagtggg	tcattatatg	aaaaagacac
10921	ttgcacacgt	acattttatag	cagcataatg	tgcaactgca	gaaatcagga	accaacccaa
10981	atgcctatta	atcaacaagt	agataattgtg	gtatacatgt	accatagaat	agtactcaac
11041	cataaaaaag	aatgaaataa	tggttggtat	ttgcagcaac	ctgcatggag	ttggagacca
11101	tcatttcta	aaagtaaccc	aggaatggaa	aaccaaacat	tgtatgttct	cacttataag
11161	tgggagctaa	gctatgagga	tgcaaaggca	taagaatgat	acaatggact	ttgaggactc
11221	agggggaagg	gtgggaggag	gagaggtata	aaagactaca	cggtgggtac	agtgttcaat
11281	gttcagggtga	taggtgcacc	aaaatctcag	aaatcaccac	taataataata	atctcttgta
11341	atatgggttg	gctttgtctc	cccacccaaa	tgtcaccttg	aattgtagct	gccataatcc

FIGURE 4-D

11401	ccacatgtca	tgggaggag	ctagtgggag	gtagttgaat	catgggggca	gttacccctca
11461	tgctgtttctc	atgagagtga	gttctcacaa	gatctgatgg	ttttataagg	ggctttttccc
11521	cctcgcttgg	caattctcct	tgctgccacc	atgtgaaaaa	ggacatgttt	gcttcccctt
11581	ctgccataat	tgtaagtttc	ctgaggcacc	cccagcccca	cagaactgtg	agtcaattaa
11641	acctctttcc	tttcaaaatt	accagtcctt	gggcagttct	ttataggagt	atgagaaggg
11701	actaatacat	cctgtaatcc	cagctacttg	agaggctgag	gcacgagaat	tgcttgaacc
11761	cgggaggcag	aggctgcagt	gggctgatat	cgtgccactc	cagcctgggg	acagtgggag
11821	actctatctc	aatgaaagaa	aaaaaaaaat	tatctatgta	accaaact	acttgttctc
11881	caaaacctat	tgaagtaaaa	aataaaatat	aacacaattt	tgtgtggtac	aaaacacttg
11941	gtaatgataa	taaacaacta	tgccactggc	ttatgtattt	actatacttt	tatccattac
12001	cttagagtgt	actcttacca	cttatataaa	aaaaaaaaaa	gttaactgtg	aaacagcttc
12061	aggcaggtcc	ctcagtaagt	attccagaag	aaaccaatgt	tattatagga	gatgacagct
12121	ccatgtgtgt	tactattccc	aaagacctta	cagtgggaca	agatgtggta	gtgcaagaca
12181	gtgataatga	tcctaattct	gtgtagccca	aggctgatgt	gctgtttgtg	tcttactttt
12241	taacaaaaaa	gttttaaaag	ttaaaaaaa	aatagaaaaa	agcttataga	ataaggaaat
12301	aaaatatttt	tgtacagcca	aacagtatgg	ttgaatttta	agtattacaa	aagagtccaa
12361	aagttaacaa	caacaacaaa	aggatataaa	gtgaaaatgt	tacagttaga	tgaggtttat
12421	tactgaagaa	agaaaaattc	tgtttatgaa	tttagtggg	octaagtcta	cagtatttat
12481	aaagtctaca	gtagtgtaca	gtaatgtcct	aggctctcac	atttactcag	cacttactca
12541	ctgactcatc	caggaccact	tccagtcctg	aaagctccat	tcagtggtaag	tgccctataa
12601	gggtaacatt	tatcttttat	gccacatttt	tattgtactt	tttctacatt	tagatacaca
12661	aatacaactg	tctacagtat	tcagcacaga	aacacgctgt	acaggtttga	agtacagaag
12721	caacagggta	tcacctctata	tagcctaggt	tcgtagtagg	ctatatcatc	ttatgacgtt
12781	cataagacaa	aatagcttaa	tgactcattt	ctcagtaaca	catagctgta	atttggttaga
12841	gcagcaactg	aaaactaata	cagatgtccc	caacccccag	gacagggacc	gctactggca
12901	gtggcctgtt	aggaatgggc	tcacacagca	ggaggtaagc	agcacgccag	tgagtgttac
12961	tgccctgagct	ctgcctcctg	ttagatcagc	agcagcatta	gattctctca	ggcacatgaa
13021	ccctattgtg	aaatgtgcat	gtgagaaatc	taggttgtgt	gctccttatg	aaaatcta
13081	gccaaactccc	actgccacca	ccaatttttg	tggaagaaaa	attgtctttc	acaaaccagt
13141	ccttggtggc	aaaaaggatg	gggaccattg	taatacagga	agagatttct	tttatttttc
13201	cttattttgt	ttttccttat	tacttactgg	cttatgaaaa	ttctacagcc	actgtaaaga
13261	ttatcaccta	cactataaag	attatcacog	cactgggcgc	agtggtctac	Rcctgtaatc
13321	ccagcacttt	gggaggcccta	ggtgggcgga	tcacgaggtc	aggagatcga	gaccatcctg
13381	gctaacacag	tgaacccca	tctctatgaa	aaatacaaaa	aattagccag	gcgtgggtggc
13441	gggcacctat	agtcccagtt	actcgggagg	ctgaggcagg	agaatggcgt	gaacctggga
13501	ggtggagctt	gcagtgagct	gaggtcacgc	cactgcactc	cagcctgggt	gacagagcga
13561	gactccaact	caaaaagatt	atcacctaca	ctaaaaaat	acctaggcct	tatgtatgcc
13621	tctttaaagg	tcacatgctt	aggacaacaa	actactcaat	ctgattgaag	aatcaaagaa
13681	agcaaaaagc	taaatcccta	ttcccctcaa	aatcatatgt	taaacagca	tcaagactaa
13741	gaaagtaaaa	gaggataaat	ctctcaatca	tgctggcctt	catattcaaa	catgccaaat
13801	ttcatacttt	atacataggt	agcacacact	ggcagtgacc	tggttttttg	agcaactaaa
13861	ataaacagca	taaggccttc	aaactttgag	attcagccat	tgtagaaat	tagtttgtct
13921	cctgaaaatt	cacactctgg	aatcttaacc	cccccaatgt	gatgggatca	ggagggtggg
13981	aatttgggac	gtaattaggt	cctgagtgcg	gagccttcag	gaatgggact	agtgccctta
14041	taagagacac	agatcaaagt	ctatgggtatt	cttattatag	cagcccaatc	tgactaagac
14101	atccatcaag	aatgttttgc	ctcagataat	tatttctcct	ccttattttt	tattactact
14161	ttgtacaatg	atcataatat	accagaataa	caataacagc	tagcacttat	atagcactta
14221	ctctatacca	agcagtatta	tgagaacttt	attcttattc	acttaatgta	tatgccact
14281	aatgagacag	cgactacttt	agtactcttt	tatggatgaa	gaaactgagg	cacagagagg
14341	ttaagtaatt	ttccaaggtc	acaatgtaaa	tggcaagggg	ggggagtgtg	aactcaggga
14401	tttagattac	agaattcatt	ccctaatac	tgtgatatac	tgctcccta	aatggggaaa
14461	aaagccccc	gaaatgtttc	aaaggYat	ttataactta	ataagacaaa	aaaagttatt
14521	acatccaaaa	ataatttgcc	ttaatcaaaa	agacaaaaaa	gtaatactaa	aaagtatata
14581	tttctagtgt	tttttctca	tctattcaaa	ttggttctct	aagcacacct	ctcctcattt
14641	ctgtaaacat	ttaatlaaga	aggcttttga	aacatacaaa	aatagaatga	Wgaactctca
14701	tgaatactta	atgctaacca	cctgcccag	ccagagtcta	ctatcctcac	tccatcttat
14761	ttcaaaaataa	atgcccagta	tcataattca	tctgcaataa	tttcagtatg	tactgaaaga
14821	tcaagtgtct	ctaaaaaaca	taaccgcaat	actgttatca	cacctaaaaa	ataaatat
14881	aataccaaat	atctagttaa	tagtcaaatt	tccaatcatc	agttaaacat	atcttcaagg
14941	atcttcttga	atcaggatcc	aggtttagac	cacatacagt	gattggttga	tctgtttctt
15001	aaatttctca	atcaatat	gcggttctca	atcaagggtga	ttttgcctct	cagggacaa
15061	ggacaatttc	tgaagacata	tttgattttg	tcacaactac	agtgggtgcta	ctggaatcta
15121	atgagtagag	gccaggtaag	cttctactta	cagggcctta	cctacaggac	ggccccact
15181	acaacaaaga	agtatcta	caaaaatgtt	actagtcca	tggttgagaa	accctgattc

FIGURE 4-E

15241	cctagggtttc	acctggttct	tttttatttc	ttacatttaa	tttattgaaa	acattaagca
15301	gtttgtcata	aaaatcttca	tgcaggtgga	ttttgctgac	tacatcccca	ggtatcattt
15361	gaaagatttc	accacacttt	atttcttgta	aactggtagt	taaactctaga	gacttgatca
15421	gattcagggt	ttgtatttgc	tttttaggtt	ttttttttt	ttttctttt	taaggcatgg
15481	ggttggcaag	actacttctt	ggatagtggt	gtatttttct	atcaggaggg	acataatgct
15541	tgggtgtatt	Sttttttagt	atctgtcagc	cactgagcct	tgatgcctag	atcccaatag
15601	cttatcaggg	attgcaaatg	gtagtatttt	aactccaaca	ttccttcttc	actcattagc
15661	tggaaatatta	ttctaataag	aacaaactca	tctattattt	gattacctaa	tagcacaggt
15721	tatatagaaa	aggcagaatc	agtggttaa	gtgagttggc	ttcctagaa	cctccaacag
15781	taacaaattt	ttgttgtagt	agtagtagta	gtagtcttag	aaattcatgg	atttagatat
15841	aattgatata	tatcaatcta	ctgaagttaa	tcttggttaa	actcaagttt	catatcctta
15901	gccagccagt	ggttagcatct	tcaagttgga	acctgaaaca	tgaccacaatc	ttaatgggtt
15961	ctgatttagta	gtttgtctatc	gattccaagc	tcagtttcag	gcctagaatc	aggcattcct
16021	ccaagggaact	ggttctttta	agtaggttgc	tgctaccttt	ttgtttttt	agctctgaaa
16081	catttgtcta	atttttaaaa	tattctcaac	catttttcat	tggtttttt	ctctctcctg
16141	aaattcttat	tatttgtatt	taggcatgct	tttctctctt	ctctacatta	tttaacttta
16201	atattttcta	ctttttaaatt	tccttcttgt	ctcctgggaa	gttctacaac	cagctctcat
16261	aattaatatg	taaattcttc	tgtagtattga	ttttaataaa	cctactactc	ttctctttta
16321	aattattctct	agcagtggtt	gaaagagagt	taatggccta	tgctggttct	ccacttgctc
16381	ctgtttatta	tctttttcaa	aagcatatat	ttgtaagtgt	gcttcatggt	ttaaaaatgta
16441	aaaatacagag	tcttattaaa	aaaaacttca	gctttaattt	tcattttattt	tcattataaa
16501	aagttaaagg	taatatatat	aagaaataaa	atcaactaaa	ataactacat	aatcacagag
16561	taaaacatgt	attctcttca	agattttatt	tacattttta	aattctagtt	agaaaaatag
16621	atactatata	caaagaactt	ttatcttgca	tatttgctta	aacattttatc	ccaagggtct
16681	tcataatagg	ctgttcttca	aaataaaatg	ctcaaaactaa	ttttaatgtg	cttagtgcaag
16741	tacctggaac	acataagttc	tgtataactg	tttattatat	cacagaatgg	tttatcccat
16801	tactaagtca	aaattaaaaat	ataaccattt	tcttctctgta	gcacattgta	gtggtttcta
16861	attctgcaat	taccatcaat	gattcaataa	ataactacat	atgttcagca	cccctcactc
16921	tgaacttcca	aattacttcc	ctgggaaaaa	tttctagaaa	tgagtacacag	gttacagggt
16981	atgaatactt	ttctaataat	ttccattaac	tcagtaacta	taaaagtgtca	tttggattta
17041	aatgtgtatt	cctttgaaata	ttagccagat	tacacacttt	taaacatctg	ttactcaaat
17101	ttccttttgt	ataataaagg	cattacagtt	taataggtaa	ctgctattac	ttcagtgatg
17161	ataattctag	tttatcctca	ctttattatt	ctttattatt	atacaggggac	catctatgct
17221	tttaaaatgt	gttatttttca	ctcataataa	taactggagg	cctataacat	tttcagtttg
17281	aattaatgaa	tattgtttaa	ttatttttaa	tcattgattct	aactatactg	atgtagtaat
17341	aatctttgac	tttcatatgt	atcttttctt	tgcttgcct	aaatttgccc	ttctttgtta
17401	atataaaactc	aagagtcttc	acaatttttc	cctccttttt	gaatttactt	taagtttggt
17461	ggcaaagaga	atcattctga	ctgtgtactt	ttagtagcac	aatttcagac	tcctgaaatg
17521	tcagatactg	aaagatgttc	cttagctata	tttttttaact	gctggtataa	tgttaaatat
17581	tcttaaaatt	tggtgctttt	caaattctat	attctacaat	tttcaaaactc	agactacaaa
17641	tattttttat	atatataaaa	tattcctgtt	atacatacac	acacacacac	acacacacac
17701	aYacacacat	ataaaacaga	ccaatgttgc	agaggtgtat	gtctctaaat	gggggtgggg
17761	gtggaagaaa	ggagataaag	agaagataga	agaagataga	aactgactca	ccttgaatct
17821	cattacaact	tcagccagta	atatattgtac	atatataatg	atattatttta	gYactactctg
17881	aagcaactag	cttagtcctg	agtctatgtc	taaatagtta	agtagttttt	ttataatctc
17941	actcatttta	tttacttttt	tctcaggtta	ctgttttatt	gatataataa	aattttacat
18001	ggtacatgtc	acattttaat	acctgtatgc	aatgcataat	gatcaaatca	gggtaactgg
18061	gatgtaaagt	atttttgaag	aagtctttta	acctatttct	ctactgcatt	atcatagaaa
18121	tgtggaatta	gattttaatct	ctataatccc	ccccagcact	aaaattctaa	tgatttggtt
18181	gcaaaccctat	attttaagatg	tttttaagta	aagaacattc	cttaaatctc	tgaatctcaa
18241	aatacagtgc	tatgcagaga	acagatatgt	tcaaataact	gttggtcgtg	tgactctaaa
18301	cagatttaac	aaataaaaac	ctttctctgt	gtgggtgtag	aatcgaattt	catttctgag
18361	aaaaacagcat	tttaattgtc	catcaaatcc	aataaatcag	agttctacca	agagtgaaac
18421	ataaaatatat	aaaaaaagta	ctcaccaata	tatcctggcc	aacatgctgc	tttccctttt
18481	cttctgtggg	tcctaataatc	aatttcccag	tagaaaaaaa	gggtgtatcc	aatgtcttgt
18541	ataccttcaa	ctcaccaatgc	tttaacaaaa	attgatattg	atcttgtggc	cttacaagat
18601	ctaggagtaa	aacagtaata	caaataataa	acaacagcag	tattgggttaa	tgatataaca
18661	tatacacata	tatataataa	agagtcattt	ctggatataa	atctgcctta	gagagtttgt
18721	tcagagcatt	aactctggag	ctagaatgcc	agaggtaaaa	tcctgtctct	gtcttaaaag
18781	ctgcatgacc	ttaggcaagt	tacttaagct	ctctctcact	gtgcctcaat	ttccttttcg
18841	ataaaattaa	ataataataa	gttcatctat	togatattaa	tgagctgctg	tgaatatcaa
18901	cgagttaatg	tgtgtaaact	attttaaaata	ttgtctggca	aaaagtagcg	actgttagca
18961	ccagctgaat	aacaaaatgg	cagttatata	ggaactgaga	cagaaaatag	aattagctga
19021	gataaaaaaa	agaattctct	atttttaaag	tttaacataa	accacaaatg	tatcatcacc

FIGURE 4-F

19081	atgccaatag	atTTTTTTTt	ctgcttgact	aataatTTTT	attaggtaaa	gtttgtgaga
19141	aagcagagtt	ctaattgggtg	ttcataaaatt	actacctcac	ttacaaaaat	ttccattact
19201	taacaaactt	ttccagatct	ataattaata	aattattctg	tcatcaatgt	ctgattctgt
19261	ttcccaggat	atTTTgggaat	gttagtgatc	ctacagacta	catgatatag	aaataaatat
19321	atatatatat	atatatatat	atatatatat	atatatagaa	atatatatag	atatatatat
19381	agaaatatat	atatagtaga	ttcaagaaac	aaataagaaa	tgaactTTTT	acaacactca
19441	caataacctg	gtagagtaca	gcaatgcttt	cagttaagac	actaaacaaa	actccatact
19501	tctaagctct	gttaccaaat	aaataatctg	catatagaga	tacctttgct	aagggtgttaa
19561	gatattaaat	gaaatctatt	ttcatggYca	aaattTTtaag	taggagtacc	attattacta
19621	cctttctttt	tttaggaatt	aactaactag	ttttattatt	attattattg	agacagggtc
19681	tggctctgca	caccagggt	gaagtgcagt	ggcatgatct	cggctcactg	caatctccac
19741	ctcccagact	caagcaattc	tctgtgocca	gcctcccaag	cagctgggac	tacaagcacc
19801	caccaccag	cccagctacc	attaccgcgt	ttctgatttg	acctaactct	cctctgatat
19861	aggacaaaca	gcccttagta	ctcaatggta	cagtcataac	agttgttaaW	atattttaat
19921	atTTcatata	tatatatata	tatatatata	tatatatata	gagagagaga	gagagagaga
19981	gagagagaga	gagagagaga	gagagMgcct	ggttgttaaa	cagttgcgta	atccataaac
20041	tcctatccca	ctatagccca	tcccttgggg	atcttacatg	acctgctaga	gactaaatat
20101	ttaatccaat	acagcaggag	gcttccagga	ctttgcagca	ccagctttaa	ggttaaacct
20161	ggcatctgta	caactgattg	atgcccttgc	tagtcatcct	cacaaaggat	tcataatccca
20221	ggtaacatta	ctgccatctg	tagggccaga	agtttgtctg	tgccctaacc	acaatccctg
20281	cctggcttca	tgataagcgt	atccttgagt	ctgccaacta	tctatctaca	attccccata
20341	aacagcctct	gttcccattg	gtcctcctgg	tcaaagaagg	cctagaccct	gttgggggag
20401	acgacattcc	tgattgtagc	actacttgtg	ccccagagga	caagtccggg	gtgttaagtg
20461	tcccctggag	ctgtctgata	tcaatattcc	cccacagttg	tcttcacata	gggtgctcgt
20521	tggaattaga	ctcttctgga	cttttagcact	gatagaattg	gggagagaaa	gggaRagtag
20581	acaggccaat	catcaagcaa	gcaatatTTT	cttacaaatt	gtttaattaa	gtattttcag
20641	tatcatgcct	gatcttacct	atgagaataa	tctctcttgt	ttctgggtcc	tttaccctcg
20701	ttggctgcaa	aggatctcca	agaggatata	ctagattttac	cattaagtta	gtctctgcaa
20761	aagaaatacc	attgaaatac	aaactactta	cttaaaatta	ttctcaatcc	caaaaagttc
20821	agtacaaaat	atagctatag	agaagttata	aaactgtcaa	acgcaaagaa	gtctcttctt
20881	atTTtataaat	cactctgata	aacaaaaatt	caaacttaaa	aaccataaat	gattttaatat
20941	aaaagcaaac	accctaaact	tcctatTTTT	tgtaagcctt	aacatgtaaa	ctcttgcatt
21001	atcaaaggat	taagtgatgt	tttgcataat	ctctaagtga	gatagaggta	tataaaacac
21061	tttagaaatg	tctatgttaa	ccatagcctg	gRcataggaa	tggtgggttt	catttgactg
21121	ggaaatttac	tcataagaaa	atTTtataata	tgctattaat	aatTTTTtaa	gaataaaatt
21181	agcttacttt	ccatttgtaa	gaaagtagac	attaaaaaat	gaattttacc	tatgggtatta
21241	tttctgaagt	ttttggaagt	aaatttcata	ttttgcaaag	agcttcttct	caaagtactc
21301	ctatTTtataa	taaaatctaa	aagttaacttt	cagaaataag	ttcatacttc	tttcatcggt
21361	atcaagacag	atccttttct	tattagattt	tttgttgact	tttccaatat	tttcttttgc
21421	cttcccttta	gacgatattg	tgtctggaga	tagtactcca	ctaatacaga	atcctcctga
21481	aatttaacaa	aaaaagtaaa	atatacatgg	gaaagacaaa	atcttgaaac	aaaactcctt
21541	aaatttaata	tggcacattt	cctttcaaag	taccaaaaga	tatatgtctg	cagctaatag
21601	ttaaaaataac	acaaatacca	accaaattca	ttatatctct	accaccctaa	atcagaggct
21661	gataaaacag	gattagatga	tgaacatga	ttagatggtc	ctattgctcc	cctgaaatca
21721	acagtcatca	gtggaggctt	ttaaaaaaa	aaaaaaaagg	aggggggctag	caatgaacta
21781	tttatagaaa	tccacatgag	tttagtcctt	tgacttagat	atatccatca	aagaaagaaa
21841	tatggccagg	cacagtggct	cacacctgta	atctcagcac	tttgagatgc	caaagcgga
21901	ggactgcttg	agcccataag	atgagaccag	cctggacaac	atagcaaggc	ctcatctcta
21961	caaaaataag	aaagaaaata	actctacgat	taacactaca	ctttcttgcc	cacctacac
22021	tactttgtag	aaaactatga	gaaaaatgaa	aatggttaat	aggaaaaata	atgaaaacta
22081	ctttaccttt	accagttaca	atTTtctcac	gttctaactc	aacgctttat	attatgcaat
22141	tggaatctt	gtcagatgat	acaggaataa	caacattcag	ctaccaaaaga	gaaaaatatca
22201	gcatctctac	attaatcaga	caaaaatgaa	tttaaatcct	attatcaaaa	tttggggggg
22261	tgatgattaa	gtaaggtaat	gtatataaac	atgtagtgca	gtgtctggca	catagtaaac
22321	aaatTTTTta	ttgacagata	ttataacata	aataagtttt	acctgatggc	cttccttgat
22381	aatctattcg	ctctcctcgc	cagtactoca	aaggtttcaa	acgtgttctc	ttggctcctgc
22441	gaacatttgg	tgtgttggag	ggcaatacta	taaaaagatg	tcagacaaaa	gtgtatacat
22501	agtttttagt	tgatggtact	tagcagtgga	aagactgtct	tttagaacat	gaaagcttta
22561	tttttttagaa	catgaatatt	tttctagaca	aaagactaga	aaaaacaaat	attttgcta
22621	acaattaaag	aaaagccaat	gaaaaaacag	gctaccaaat	tggaacaatat	ttaaaaacct
22681	aataatactc	agcgttgaca	atgttaaatg	tacactcatc	ttatctgaac	aatgcaaagt
22741	tctgtatact	aaattgagtt	tgtttgctta	tcttcaaatt	cccattgtct	tacctatttt
22801	ttgtttgcta	aagctatgct	gaagctaacR	agaagttgcc	tactgctctt	aggcataatg
22861	ctcaatgttc	ccctctgtaa	atactgaagc	cctgctcagg	aacattttta	tttccctttc

FIGURE 4-G

22921	cctactcctg	attcatcatt	tcaccccaag	acaagcatta	agtattgaga	ggtatagcag
22981	tctctcatca	cataggccca	caaaatactg	acaatatcta	agttctggag	taaggcaatg
23041	agagaaagct	tcactcctat	tggtaatctg	agtatgagtg	aaagagcact	cacagcctca
23101	aataaaggga	gaaacatgga	aagccaccca	acatcacaga	aaggtgggaa	ctatcatgta
23161	tcttgactgg	caaatatctc	tttgggaacc	atggattggt	aatctttaca	tgggcctctc
23221	catgggttcc	acagttctta	gctttgtcta	cttactatcc	tagctactgc	tttgtttagg
23281	agtcaactgg	attaaagtgg	aaggagatgc	tgtcaaggaa	gccatctacc	tggtagttac
23341	agtttctttg	acaaaattct	ccaccctagc	ttcatagcta	agggaggatc	atgcccccta
23401	ctatggggca	aaaagtgaga	gggcaatagg	atttataaat	ggacaataga	ctaaYtcaag
23461	tggcttgtgg	tgacttacta	tgaaattcat	aaaaactaag	tgcataattt	taattttatct
23521	gccaattaat	ccacataatc	gtatttctcc	tgcttaagaa	gaaataagtt	atattttagaa
23581	acagaaaactt	aagggtatttt	tctcaatgaa	aatattaaaa	aagaaaaata	ttcttaccta
23641	gtttgtgatg	gattctgttc	tttgggtatca	cttttagattg	ttttgagtca	tctacaaaat
23701	gcaaaagata	atatcRtaag	aaatgactgc	taattccatg	ttaaattaaa	atgtgtttcc
23761	tgggtcaattt	cagtatgagt	atttttaata	aagtttgacc	tgataatgta	ttttattact
23821	ccttttgcctt	ttcattgctc	aactataaaa	actaaggaaa	agaactatct	ctctagactt
23881	tgctacaatK	aatacattgc	aagtttgtcc	aatccacctt	attttgtggt	tgttctgttt
23941	tgttttgttt	tagaccttta	gcagcctgaa	accatgcttt	ttagtttctg	tctctggcga
24001	Yaagtggaaa	agagggatga	ggaaggggtt	ttattggacc	aaccagaaac	agaaactaag
24061	aactcatgac	tgtattcgct	cccttggaaca	cccttggttt	ttattctaaa	cagtgttaaca
24121	gttaaaacaa	acaaacaaac	aaaaaaaaca	acagattttc	tattgctcat	ggaaagatga
24181	aataagccac	ttgtggataa	aaatgtaggg	cctgataatg	gataattaat	atgctattta
24241	tgaactatct	tgaactttct	ctttaaagtt	ctaaaatagt	gtaagtgtac	tgaatttagc
24301	agtgtgccaa	taagctcagg	ggttctcaac	tttggttaact	agcacctaaa	gatggctgtc
24361	atcccttctt	tgcccttcta	tgacacaaatg	ttctgtatca	agaagcagag	tctcgttccc
24421	ttctccttca	atctctgctg	gagtttagtga	cttgcttaac	taatagtatg	caacagaaat
24481	gatgttctgg	ggcttaaaaag	gctaagtcct	aatacaatct	acaggttcca	tctagaagtc
24541	ttgggatctc	actctagggg	aagacagcaa	caatatgaag	attaacacaa	gactgccatg
24601	ctgtgaggaa	acctcatgtg	gccacatgga	aaagccacat	ggaggaaaag	agatgcttgg
24661	ccaacctcaa	tgtcccagtt	cttccagctg	ggtccaaaca	tgtaaagtga	gaagttacct
24721	cgaatgtcca	acccatttga	actttcagat	gactccagcc	ccagcagctt	gcatttaact
24781	atataaattc	atgagtgtac	tcaagtggga	attacccaac	taagccaagt	caattcatag
24841	aacctgaaa	gataaatcaa	tcaactgtatt	aagcctttta	gttttgggg	ggttggttac
24901	gcagcaatat	acaactggga	cacaattgtcc	atgaaccacc	taaaactgca	aatacaattt
24961	tgtatgaaat	atataccttt	tttccctaaa	aagcRgggtct	gagcttttat	catatttctca
25021	aatgagtcca	tgaagcaaaa	caaacaaaaa	ttgttaagaa	tgattgaatt	agatatttta
25081	taaaattgct	ggtttggaag	aaacttcagt	gatcataaca	tctaatttcc	ctgtcagaaa
25141	caggcaaatc	tctagacatc	agaagtagat	tagtaattgg	gtaggcccag	ggaaaggaaa
25201	tgaaagtcgg	ctactaaagg	gtaaaggggt	ttctttttgg	gggttatgaa	aggttcttaa
25261	catcgattgt	gtcaatgact	acatatcatt	gatttgtaca	ctctaagtgg	attaattata
25321	tggtagtgga	agtctagctt	aataaatctg	tgtaccccc	acccacccc	cacccccacc
25381	cccaaaaatt	caatttctta	tgcagtctcc	cctagaacaa	gtagaggtct	catctctgtt
25441	ggaaattctc	ctgtgacact	ggcctcgga	ggcagtgtca	gagtataca	aggaacaaaa
25501	gaaacaagta	aatatactga	ggataatggg	agtcaggttt	ctcactatct	gagaagcaact
25561	tgtaataaat	acaggcggcc	aggcgcagtg	gctcacaact	gtaatcccag	cactttggga
25621	ggctgaggca	ggtagatcag	gaggtcagga	gttcgagacc	agccttacca	acatggtgaa
25681	accccatctc	tactaaaaac	acaaaaatta	gccgggcatg	gtggcacacg	cctgtaatct
25741	cagctactca	ggaggttgag	gcaggaagaat	cgcttgaacc	cagaaggcgg	aggttgcaat
25801	gagccgagat	cacaccattg	cactccactc	tgggcgacag	agggacactc	cgctctaaaa
25861	aaaaatttaa	aaataaataa	ataaaaaatac	aggcatacct	cagagatatt	gccagttcag
25921	ttccagacta	ctgcagtaaa	acagatactg	caataaagaa	gtcaaacagt	tttttagttt
25981	cctggtgaat	ataaaagtta	tttcttttgc	tgttttgttt	tggttttttg	agactaagtc
26041	tcactctgtc	ctgtgacact	cagtcgagtg	gtgggatcaa	gactcactgt	ggcctcaact
26101	tcttggcagc	aaatgatcct	ccgcctcag	ccgcgcagtg	agccggaacc	agagatgcac
26161	accaccacgc	tcagctaatt	tttgtatttt	ttgtagaaac	aggtttctgg	catgctggcc
26221	aggctggtca	caaactcctg	ggctcaagtg	accggcctcg	cctcccaaag	tgttgggtgg
26281	ctcccaaagt	gagccaccat	acccagccaa	aagttatgtc	tatactatac	tatagtctat
26341	taaatgtgca	agagcattat	gtctaaaaaa	atcagtgatc	atatacctta	atttaaaaaa
26401	attttattgc	taaaaatgct	aaagatcagc	caggcatagt	ggctcatgcc	tgtaaatcca
26461	agactttggg	aggcccagga	gggtggatca	cttgaggcca	ggagtgttag	acaagcccga
26521	ccaacatggc	gaaaccccat	ctctactaaa	aattaaaaaa	attagctggg	tgtgggtggtg
26581	tacactttgt	aatcccagct	actcttggtg	gctgcggcaa	gagaatcgct	tgaaccaggg
26641	aggtaaaagg	tttcagttag	ccgagatcac	accactgcac	tccagcctgg	gtatttagagc
26701	aagcctctgt	ctcatttctca	aaaaataaaa	ataataaaaat	ataaaaaatgc	ttatcatctg

FIGURE 4-H

26761	agcttttcagt	gagttttta	cttttttgc	ataggggtatt	ttgccttatt	gttgatgact
26821	gctgactgat	caggctgggg	tgtctgtggc	agtttcttaa	aataagtcaa	caatgaagtt
26881	tccctggaga	atataaaatg	ctgttgtata	gcattttact	cacagcagaa	cttctttcaa
26941	aaccgcaatc	aatcctctca	aactctgtcg	ctgctttacc	aaactaagttc	atggaatatc
27001	ctaaatcctt	ttttgtcatt	tcaagggttc	acaacatatt	caccaggagt	agattccaac
27061	tcaagaaatc	agttccttcg	ttcttccata	agaagcaact	cctcatctgt	tcaaattttg
27121	tcataaatt	gcagcaattc	agtttcatct	ccagactcca	cttctaattc	tagttccctg
27181	gctattttcca	ccacatccag	ttacttcctc	cattgaagtc	ttgaaccctt	caaaatcacc
27241	cataagggtt	ggaatcaact	tcttccaagc	tcctgttaat	aYtgataattt	tgacctcctc
27301	ccatgaaaca	caaatagttt	taatggcagc	tagaatgggtg	aatcctttcc	agaaggttta
27361	tttactttgt	ccagtcccat	cagaggaatc	actacttgtg	gcagctactg	ccttacaaaa
27421	tttattttctt	aaataataag	acttaaaagt	ccaaattatt	ccttgatcca	tgcatgagct
27481	gcagaatgaa	tgctctctta	gtaggcatga	aagcaacatt	aatctcctca	tctttgtcca
27541	ttagagctgc	tggtggcct	ggtgcattgc	catggatgtg	ctgtcaccca	ggctttgttg
27601	ttctactaat	agagcaaagt	agattttagca	taattcttaa	ggactctagg	attctggaa
27661	tggtaaatga	gcactagctt	caacttaaag	tcaccagctg	tattagccct	taacaagaga
27721	gtcacagcct	gaccttggaa	gctttgaagt	catgcattga	cttctcctca	gctatgaaYg
27781	tcctagatga	catcttcttt	caatagaagg	ctattttgtc	tacagggaaa	atctgtgtt
27841	tagtaaagac	accttcaatt	atctcagcta	gattttctgg	ataacttgtc	gcaacatcag
27901	accttgctgc	ttcaacctgc	tcttttatgt	tatggaaaca	gcttctttcc	ttaaacctca
27961	tgaaccagcc	tctgctagct	tcaaaactttt	cttctgctgc	ttcctcacct	ctcagctcc
28021	acagaattaa	agagagttag	ggccttcctc	tggattaggc	tttggcttaa	aggaatgctg
28081	tggttgttt	aatcctctgt	ccagaccact	gaaacctcta	tatcagcagt	aaggcagttt
28141	ccctttctta	tcattcatgt	gttcactgta	gtagcacttt	tcttttctt	caagaacttt
28201	tcctttgcat	tcacaaattg	gctgtttgtt	gcccagggcc	tagcttctgg	actatctcgg
28261	tttctgacat	gccttcctca	ctaagcttaa	tcatttctag	cttttgattt	aaagtgaaaa
28321	atgtgtgact	ctttctttta	cttgaacact	tagaagccat	cgtagggtta	ttattggcct
28381	aatttcaata	ttgtgtctca	ggaaataggg	aagcctgaag	agagggagaa	agatggggaa
28441	ctggccagtc	agcagagcag	tcagagcaca	tgaattttca	ctttcttaag	tagctgtggt
28501	ttgcggtgcc	ccaaaacaat	tacaatagta	atgtcaaaga	tcacctgac	acaaatcacc
28561	ataaaagaca	tagtaatgaa	aaagtttgat	atactgtgaa	aattaccaa	atgtgacaca
28621	gagacacaag	gtgagcacat	gctattgaaa	aaaaaaatgg	tgccaataag	gcttactcaa
28681	caaagggttg	ccacaaacct	tcaattttgtg	aaaaatgcag	tatctccaaa	atgcagtgac
28741	acaaagcaca	ataaaacaag	gtatgcctgt	ataaatataa	atatagaaat	agatatagat
28801	gcctgtattg	tatatggtgt	gtacatatgt	gtatgtgtgt	gtgtatatat	atatctattt
28861	cctatctctg	tacactgaga	aagactagaa	gcaatgggtat	cccaaacaag	gatcacgtca
28921	agtgcccaaa	tcttggtttc	taaatgccat	cttccactaa	aaagaaccag	gtttcctgga
28981	gcagtaattg	atcccagagc	tggggcagga	aaaagactgg	aacatcttat	gccccaaaac
29041	aaagacagta	ttcacagaat	catgacaaaa	gcacacagag	accagctgaa	agaaaaatSa
29101	gtgaccaaat	ctatcacaa	tcaagtatca	taataaatgg	tcaagatttt	acaaatccat
29161	ggcataaaat	agtagtagtc	catactgata	taaataaaaa	gaatcatgaa	taaaataatt
29221	ggcatgcggg	agaaaaactg	gcaactaatt	aatgcggaag	gaattaaaga	aaagaaaat
29281	agaaaataat	gtggtaccat	catttagtggc	tgataattca	agtgggagtc	ttgaatgtat
29341	gttaagggtg	gtgaatggag	gtttgacaag	aaacaggcta	ttaagagtat	cagaatatca
29401	ctccacaata	atattttatca	attataagag	aaaagcagtg	tctttacagt	agagaaacct
29461	ggcagacaat	aacatgaaca	ggtaatcagg	attgatatca	tgtcagcagg	gcatgggtggc
29521	tcacacctgt	aatcccagcg	ctttgggaga	ctgaggtgtg	cagatcactt	gaggtccaga
29581	gtttgagacc	agcctggcca	acaaggtgaa	agcctgtctc	tactaaaaat	acaaaaatta
29641	gccagcatg	gtagcatgtg	cctgtaatca	cagctactca	ggaggctgag	gcatagagaat
29701	tgcttgaacc	tgggaggtgg	aggttacaat	gagctgagat	cacacaactg	cactocagcc
29761	tgggtgagag	agcaagactc	catctcaaac	aaacaaacaa	acaaaaaaca	aaagcatcat
29821	gtagatgggt	gaacgttgtg	tgcctcctgt	gtgatgcaca	aattacatcc	cctaactcct
29881	aaccctatag	catcatttct	gtagtattcc	tgtcaaata	gaatggcaca	catttgatca
29941	tgagttaagt	taggaaaaaa	actaagaaac	tgttccatgt	tgaaggaaac	taagggacat
30001	ggcagctaaa	tgcatgac	gatccaggac	tggatcttga	accaggagga	agaagaaact
30061	ctgagatcca	ggactggatc	ctgagctaga	agggaaaagg	aactgctagt	gaaatctgaa
30121	tggagtctgt	gaatgaacct	gtgtgttatt	aatgctgatt	tccttatttg	tatggttcga
30181	gggtagttat	atccttgtct	tgtgaaata	cattatgggg	catttaaggg	aaataatata
30241	tcattgtctac	aattcctctc	caaatagtct	agaaaaaaga	tgtatgataa	tagacgtgta
30301	tttattagag	gaggcagggg	gggagatgga	aaaatgttgt	aaaatgtgga	caattgtgaa
30361	atcttgatga	aggggatatg	ggatctctgt	ataagactga	aattatttca	aaataaatta
30421	ttttttaagt	gactaacaca	agggacaact	cctaaatttc	aaagattaaa	ggatcctagt
30481	agtatggag	atggaagaaa	acaggttatc	tacaaaggaa	agaagaaata	aggctgcctt
30541	caaatttcta	ttcataagca	ttaactctca	tgaagcaaaa	tagcaatacg	gtgatagttt

FIGURE 4-I

30601	aaagaaaaaa	agatcatgac	tcaagattat	gttctctatt	tagctgggtg	ttcattgtgt
30661	ttaaaaaaga	aaaaaaaatc	ctgagtcctt	gctagaatat	gtgagaatgt	ctaccaactt
30721	tacaaagaag	taacaagtat	atctgttgac	aataagtgta	tatatattaa	acaattttatt
30781	aaaggaaaaa	gtactgacac	agcgagtcaa	aaacaattca	atcatatgct	gtttcttagc
30841	cacttttaaat	tctctaataa	aagttaaata	aaaagataaa	gaaacaacaa	ccaacaaaaa
30901	gaaagcagaa	gtcacaatac	taatattaga	caaaacaaac	tacaaagtaa	aaagcatttta
30961	acacaacgaa	gcagataaat	ttgaccaaag	caggtaacct	ccatatgaag	gcttatgtga
31021	tcagtaacag	cactgaaatg	tacataacaa	agactacaga	aaatacaagg	gcaaagacag
31081	ttgcagtggg	aacactttac	ttcaactcta	gcagtcctta	atagatctca	aataaaaaaga
31141	atacataggt	tgagaacatc	aagcttagta	tgccaaatc	taacRtcctg	ttcttttctt
31201	caaaatctgc	ttcttcccca	gtagtcccca	gatcaggtag	taatattgcc	attcttccag
31261	gagctcgggc	caaaaacctt	caagttctct	ctaacgcctc	tctttttctt	atacaccacg
31321	tatcgtccat	cagaaaaatcc	tggtgacttt	accctcaaaa	atacctaaaa	atcctcctcc
31381	tgctttccac	tttctactgc	taccacattg	gtctaagcca	acacctctca	ctaggattat
31441	ttcaacatct	ctccagctag	tctccttgct	tccaaccttc	ctccatccct	tcaaccccat
31501	cagtcaactc	ctaacacagg	agctgcagtg	attctgttaa	tacaggtaa	gtcatgtctc
31561	tcttctgctc	aaaaccctct	aatggcttcc	catcgctctt	agtaaaattt	tgcttttaac
31621	atcctatgtg	atcttttcatt	ctgttgccctc	tgtagacatca	tttttcttac	tactcgttcg
31681	ctctcttcct	ctgctctaac	cctctggcct	tcttggtggt	cctcgatcaa	gacagactct
31741	tgaccacata	agaacttttg	cccttctatc	tccctctacc	tggtacacta	tttaccaga
31801	cagctgcacg	gtttgctgtc	tcactctctt	aaatctttgc	tcaaatgata	acttctcttag
31861	tgaggacttc	tctgcccata	tacctaaaaa	tgtaaaactt	atttcccacc	ctaaaagcca
31921	tgctttattt	ctctactctc	aacacccaac	aatcataaaa	tttggtatct	ttttatattg
31981	tctgccatcc	tgccccttcc	agaaatttaag	ctggaggggc	gaaatttttg	tcagttttgt
32041	tactgacac	acccctaccc	ttaaaataat	aagtaaatat	tccataattt	ttcatattta
32101	agaattccat	aaatattaaa	agtatattca	aaaaaatata	tccacttatg	ttatcaacaa
32161	aataactgga	tatatatctt	taaatccata	tctgtataca	aattattccc	tttttcaagc
32221	accaatggaa	aaattataaa	aactaagcat	acactagaca	ctagaacaca	aaaaaaactt
32281	actgaattca	aacaataaat	aaaatagact	aagttttcta	gaacaataaa	atgaaaccag
32341	aaaatactaa	aagaacaaaa	taaaacacaa	cttcttagaa	taacagcaaa	aattggctat
32401	ttacatata	cctgatatta	aactaagcaa	agaatatgta	ttcatcttta	tatcagctta
32461	tgggattgga	gctgatata	ttttacagat	aaggaaactg	aagtttaaga	acactgaaat
32521	ttcttactca	agataatata	gtgatgtctc	ccgatcagtg	gtgaatgggg	caaaaaaaaa
32581	aaaaaaaaag	aacgtagcta	gtaagttagta	gagctagaac	caatcccagg	tccatgaccc
32641	tgagaccaa	gctcttaact	aatgtactct	taaataactg	ctgggtcaaa	gaaaaatcac
32701	tacaatttag	agtatactac	aataacacta	catagcaaaa	tctatcaaat	taagccaaaa
32761	ctatactgag	ggaaattgaa	tgctgcttct	ttaccaaaga	aaaagcagaa	aaacacagaa
32821	agcattcaag	ttaaaagaga	aaatacaata	aatctaata	cgggggaaaa	attaaaaagt
32881	taaaagaata	gtgattatta	gaaaaaaaag	tataacagat	tacaatcaag	cacgcatttt
32941	taggagcatg	aaaaaattat	aaaattctct	attaagaggc	atcttttaaac	ttcagtatga
33001	aaattttcaa	gtactgaagg	ccgggagtg	tggtcacac	ctgtaatccc	agcactttga
33061	gaggctgagg	cagggtgatc	acaaggtcag	gagtttaaga	ccagcctggc	caagatgggtg
33121	aaaccccatc	tctactaaaa	agacaaaaaa	attagccagg	cgtggtggca	ggtgcctgta
33181	atcccagcta	ctcaggagtc	taaggcaggga	gaattgcctg	aaccaggag	gtggaggatg
33241	cagtgaagctg	agattgcacc	actgcactcc	agcctgggag	acagagcgag	actccgtctc
33301	aaacaaaaaa	aaaaaggaaa	ttttcaagta	ttgaaaatag	agaaaatagt	ataatgaacc
33361	caatacaacc	atcaaccagc	ttcagtaatc	atcaacagat	cactaatctg	cttcatgtat
33421	acccttatta	gcttaacaat	tttaaatact	ggagtagaca	ccttaagtgc	caatatttca
33481	ttatgttcta	cttaaaaaac	tgctactcat	tttctttctg	tctcacttag	gtacagggtc
33541	ttattaatct	ctaactaagg	gtcttaagag	gtaggtagtc	aatatacact	cgccatcagt
33601	gacaatgtaa	acaaaacata	gcactcctta	ctccatattc	ataatgccat	aaaaatcaag
33661	acagaaaaaa	aacaatagtt	tacctgaact	tccatgaact	tcctcatcat	ccacatcatt
33721	ctttccagac	attaaataat	tattatttag	cctggaagg	ccacttaaga	aaaaaggaa
33781	accacaaaaa	taatgctttt	ataatacata	tatctaagt	atttgcctta	atgatcattt
33841	ttctcctaaa	actgccataa	gtctttctta	taaaaccaat	agtgatgta	caagtcata
33901	aaaatatata	gtcatocctc	agtatttggt	ggggattgat	tccaggatcc	actgtggata
33961	ccaaaatcca	aggatgctca	agtcccttat	ataYaattgg	gcagtatattg	catgtgactt
34021	tcacatatcc	tctgtatata	tttaaatcat	atctagggtta	ctgataatac	ctaatacaat
34081	gtaaatgcta	tgtaaatagt	tgttatactg	tatttttatt	tgtattattt	taaattgtcat
34141	attgttactt	tttattgttt	tatattttat	tttctgaata	ttttcaatcc	atgggggttg
34201	aatcagtgga	tgacagaacc	acagatatgg	agggtgact	gtacttgctg	cattaaacaa
34261	agactacaat	ttcatcccat	aactgacagt	tgagcatcat	aagtactgaa	tttatgactt
34321	acagatcaga	gtaacagact	tagtaaatcc	aaatgataac	atcctgtggg	gaaaatcaaa
34381	ttataaaaaa	agaaagaaat	catcatattt	taattaaaaa	aaaatatagc	caaaaaccaa

FIGURE 4-J

34441	tgggaatttaa	aatgtggtcc	agaaattgtc	agagatgatt	cagcctctcc	tagtcctaaa
34501	tctcttttcta	cctattatga	acccaggata	agcctagtca	taacctcaca	aatagtaaag
34561	aaatcttagc	catcccttaa	aagtctgaga	atlttgctaaa	atlttagcctt	tattcattttt
34621	ttaaaagggtt	atatgacatc	agatataatt	aagagtaggt	aattcaattt	gatcactaaa
34681	tgtggtcatt	ttaacattat	atgtccaaat	tctttaatac	accacctttc	aataggtgga
34741	gcctaattcc	acctctccct	gaatgtagtg	tggactcaat	aagttgtttc	taatgaacag
34801	aataaagtag	aaatgacggg	gtacaatgtc	aaagactaag	tcattaaaag	acactgtgat
34861	atccatcata	gtcacacctt	ctcttggagc	atlttgctttg	tgggaagcca	gttgccatat
34921	tcagcagctg	agagggccac	aYggttaaga	aactaaggtc	tactggaaac	agccagaacg
34981	gaactggggg	ctccagccaa	cagcgatgtg	agacatttta	taggtggatt	ctocagttcc
35041	agacaagact	ttaaaagggtt	aaaaccagaa	agatgactgc	tacctcctga	gaatatccga
35101	gccaaaacta	gctagctaag	cctcccagat	tgctgaScCa	tagaaactat	gaaacaataa
35161	gtgttttttaa	gctttttaaca	aaattaaaaa	aaagttcttg	ggtaatctgt	tatacagcaa
35221	tgggtaacta	atatatacaa	ctattatcct	tacaatacac	gcataccttt	cctctaaaac
35281	tgaagtctta	tgctctccag	aatccaagtt	tgactctgtt	ggatatattac	atgtatatcc
35341	actggtctga	ggcttttaggg	gaacattctg	tgcagtcata	atgttatctt	cattcttttga
35401	gcttcttgta	gatctataaa	aatgataaat	gtatgagtgt	ttatacttct	tcaaaataaa
35461	atlttcttcc	agaaacgata	cacaggtggg	tacaaagaca	atgtaatat	ggctataacg
35521	aatatcagat	cacctgttcc	agttcttgag	acttgcaact	agctaaggaa	ggaaactggg
35581	ttctaggacc	taccaagagt	cccaatttga	aaaattctga	tgagagaaat	ggagaagaca
35641	cctgccaaag	aaggtggtga	aaggacata	aggagacctt	atctataagc	agcttgatat
35701	atattacagt	taatctatca	tgttttactg	gagaatccat	aaacaactaa	aattggcttc
35761	tttgatatcc	ctagtccagc	tactgagggg	caataggggc	ctcagaggga	ctgagctcat
35821	ctctttggta	gttagtttac	tccaaatata	tgcaaacaga	atacactctt	cctagtgaact
35881	gtataattct	tcaggttcta	gtatcctcct	gggtcctacc	attaaagtca	aaagaaataa
35941	aagtgattac	aagagaatac	taggaacaac	tgtatgccaa	caaattaaat	aacctagatg
36001	aaatggacaa	actcctagaa	agacacaaat	tatcaaaatt	gattcaagag	gaaacagtct
36061	caaaatacca	tgaatcagta	atcaaaaaca	aactacccat	atagaaaaagc	tcaggcacag
36121	gtggcttcac	tgctttttacc	aaacatttcaa	agagaattac	gacaaaattat	tcacaaaccg
36181	tttcaaaaaa	tagagagata	atacttccca	actcattgta	taaagccagt	attaccctga
36241	tacccaaact	aaacaaagac	aacagaagca	aagcaagcta	ccgatcagaa	cccctcaaca
36301	aaatactagc	aaattccagc	aaacaaataa	aataaaagag	agagaaaaagc	agagaatggc
36361	ctgaaaaagt	gaaacagaat	gggtatggga	tttctttatg	cactataatg	atatacgta
36421	atataattta	ggacacactg	tcattttattt	cagtatatcc	tcagcacctt	actgattcca
36481	acacaaagta	tgtattacct	caatagggtg	ttggaaactaa	taagaattca	ttaaaagYat
36541	ctagcaaata	tttggcacat	agtatgaact	caaaaaatgt	taactattat	catcctaaga
36601	agaaaagtat	taagctatat	tcctaactat	tgaaatcaca	ttaatctcac	ttaaaaggaa
36661	acaatttgaa	ctatacactt	aaaaaagatt	aagacagtaa	atltttatgtt	atgtgttttt
36721	tgtctgtttg	ttttttgaat	ctctactttg	ggagcccaag	gcaggagaat	cacttcacac
36781	cagggcgttca	agacaagcct	aggcaacaaa	gcaagacctc	atlttctcaa	caaattaaaa
36841	aattagccag	gtgtgggtgg	ccacacctgt	agtcctagct	actcaggaag	ctaaggcaga
36901	aggattatct	gacccagaag	tttgagggtta	cagtgggcta	tgatcacgcc	actgcactcc
36961	agcctgggaa	acagaggaag	actctgtctc	ttaaaaaaa	aaaaaaaaaa	aaaaagttta
37021	actcttggat	gacaataata	tcttatttaa	tttaacagtc	ataattccag	gtgctatgta
37081	ctattcccta	ttttaatatg	aggaaacaag	tgacaggtac	tactttgcct	gtgtgtcaYc
37141	cagctaattg	tagaggctgg	atttaataacc	aggtatgtca	gagtgcagag	ctcttcatgc
37201	taattactgc	ctgtccataa	atgactaaat	agcacaatt	attaaatgct	gaacaacaaa
37261	agtaactata	ttgtacacat	aacagacatt	acctagaaca	atcaagattt	ttcttcttag
37321	ccaagtctgc	ctcatcactt	tccaatggct	cactcagYga	acatctggaa	atttcatcat
37381	gaccaacgat	acctccagaa	ccttcagcat	ttaaaaactt	ctgtactctt	tggttgccctt
37441	tagttgctgt	cttctgcctt	ttaaagtgga	tagttttttt	cctaataattc	ttagatgact
37501	gatttggttt	cttagtagat	tttcgggtac	tattgtgtatg	cattggtaat	tcatttctta
37561	ctgaagaatt	gctataaaca	ggacctgaag	gattcaatga	taacctaaag	ttagtaagtt
37621	tgtccagatg	atlttggtca	ctgaaatacc	aacagcattt	atatttgcac	ataaacatat
37681	acacatacac	acacacacac	acacacacac	acacacacac	acacacacac	acacatctca
37741	ggctaaattt	atlttccaaat	taaattcttt	aaacaatgta	gctcttcagt	ttatagatat
37801	atgaaacagg	cccttcaaat	ctgtcacagg	cttcaagaaa	cactctctgg	ctctgcccac
37861	tgcccttctg	gccatcctta	atatctgata	ttccccaagg	tgacagcttc	agctttttcac
37921	tccatatact	ttcattgacg	gacttatcta	cccagagctt	taattactat	ctatatgctg
37981	acacctataa	tatccatcta	ctgtctctcc	ctatatctgc	ctctcttgct	ttatttctcta
38041	tcttaatgaa	aaatacaact	acctattcta	tccagatatc	taaatcagaa	atlttgagtca
38101	tgcaagacta	ctactcctat	ccacaatcac	gccctaaatc	ccatcaattc	tactttatta
38161	atgcctttca	aatctttcaa	gctctccctc	ctgtcattag	tagaagtcct	cattattttca
38221	tatctggatt	attaaaacag	tctctttact	aatctccccc	tcctagcct	tgtttttctt

FIGURE 4-K

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38281 caatccattc cctacactgc tgcaagaatc acctttggaa aacaaaaact ggatcattac
38341 aactctgctt aattaaagta ttttagttat tatctatagc ttcaggatga agtccaaata
38401 cttcaacatc aattcatatc tacatctaga tttgcttatt tcataaacca caattcccaa
38461 aacccccctc caaacaaca aacaaaaaa agccatcagt aatgaacaat ctacagtttc
38521 tctaaagcac tgggtgtcca aaggcagtct ctagaccagc aagatcagca ttatctggga
38581 atttgaaatg taaattatca tgcctcacct cagaccccag tgaatcaaag actttgcaga
38641 gcagggccca gtaacctgtg ccttaataagg cccccagac aattctaaag cactactaat
38701 taaagaaaga aaagatcaag ctctctgctc cagatctctg cacaagctac ttctacttaa
38761 aacattccat aacttcctcc ttactccact caatcactta gctaactcct agttcatcct
38821 tcaggaaRct ttccctaatt tccaagtctt aggtagcttg ctatcacaca tacgactggt
38881 tacttatctc tacttctctc ctccagcaga ctaacaactc cttgacctca agtaattgat
38941 tgggtatttta tctatgtata ttcccaatgc ctaatgacag gggcaggact atgggtgaagc
39001 aagagttagcc tcagctggaa aattcaagaa ggtactcatt ttcaggtctg tgcaagtaca
39061 gagcccgaac tgatacaatc ctgtgactga ctgccttaa tttttcacc tagtgtctca
39121 ttgtcttacc ctagtccctg tccacttta cctcattcct gccccatggc aagtactcca
39181 tatacatttc ttcatatata tgggaaggga acagtgtcac acgtacgaca ggcaggctgg
39241 gggcagggtca agttgttctt cttaaacttc gacttcagtt tcttcttcca tcagatgaga
39301 gtttagacta tatgatata aaagattcct ccactttttc gactcccagc ttgatcaaaa
39361 atccaacatc tatttcagga ctcttaaata agtgtttttt gatagtttca gagacttagc
39421 acatttatcc aagttctgta agaatttatt taccatctg tttatgtat catctgccac
39481 atagtactta gcatttcagg caacctgggg cagaaaagtg agttcccaa agcagtaaca
39541 gtattatttta acacttcaat actaacatat gccacctact atgctaattg catttaaacc
39601 ttataaaaaa tcaatgaggt aatcatgtta cagaatgaga aactaaacaa agcaatctac
39661 tcaaaagtga agagtgtac ttgtgactca gatctcact caaaatccaa aggcgtgaac
39721 aaaataaata ctgtgtgcta tccatcaaga atctcaatga tttaataatt catagcaata
39781 aggcctcaca tatacaatgc catagtgtga ctaatcattc acttattaat ctaaagccc
39841 caaagtcaat agtatttgtg tatgtgaatg ctaccttatg atccaccaat cttttcagga
39901 tcactttctt taaaaaggga caattctccc aaacaataa atgtttcata ttgtgcagaa
39961 aaaagttagc aaagcaggtc tgagtatact acccttaaaa gggcctgctt tcaaagttag
40021 ccctgtaaac tttaaatttca ggattgttcc cgtcatttcc taattggcaa agtgggtgtt
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40381 tcctttcact gtaatgaatc acagccatga gtacaactat atgcccagtc ctctagcaa
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40621 aactagaatg caagctccat gaaagcaggg atttctgggt tgggggtttg tttccaca
40681 gctattatcc ctattcctaa aatactgtat atattaacgc ttcaaggaat atctttacca
40741 ttgattttaa attcctttt atgacccaat ttaacttgggt cctcatgata ttctctatat
40801 agaaatataa aatgcacct acagaatgat tttgtctatg aacaacaca
40861 atttaataaa aaatacttac tctctctgta ttttaccacc caccaatcag atggcgctt
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40981 ggactcactg gaaaagcgct tctttttaga ttcttctta tcttttctag tgctactttt
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41101 agaaaaccac aagattataa aaaaaccgtc aattacagga acttcttaaa tttatcctgt
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41341 ctataacgtc ctaagtaaaa gtaggcaatt actgctttcc tgttttga aaatgatttt
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41941 attatagagc gcatctttca agtatacttc cttcatatgt cttttcctaa gaaattatgg
42001 ataaatcaaa attttgtatc cttcctttta atcctatgca tgtatgtata ttatctatta
42061 ttctacagaa cccaccagaa tgatcttgtt aacagtagaa ataattgggtt agtaattttt

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FIGURE 4-L

42121	gtgattacag	tgccaatgc	agtgtatggc	attcaacaac	tggttagacac	atgagtgaat
42181	gatggaagag	aatggacttt	tatctctata	aaaaatagtc	ccacgggtacc	ctgggattttt
42241	ttttaacatt	tttatttttct	aaataatttta	tcattctgtc	ttattcatct	tcogatacta
42301	acttgttttac	tagccttttc	ttttcacttt	gccctctata	tatactgcc	tctcacaaga
42361	taaacaaaaa	ctatatgagt	tagaattaaa	ttatatataa	aataaaaaag	ttctagaaaa
42421	gaacctatag	gcttttcagg	ctctttgttc	atthaggttt	actttgccta	cttgccaaag
42481	ctaagttagg	atattaaaaa	acataaaatg	ggtagaataa	tgctcatggt	tatatttaaat
42541	ataaacactt	accacacagg	ggcatctgtt	ttttggaaac	acaatcattt	cccatctctt
42601	catgctcttc	catatttctg	tctgaatttc	tttgaaattc	gtcttgggta	atatgtgatg
42661	tatgtatggt	ttcatcttta	gactgtccca	catcaagctg	ttcttcagct	ggtttagcca
42721	tgaattttct	tctctgtttt	tgttttatag	tccttttgct	tctagatggt	ttttctgcat
42781	tcttggaata	catttcatat	ttgttagatc	tataattatt	tactgtttca	Yctatcaaag
42841	cataacttgt	atccagttact	gttttatcag	agggctgaga	tgctctctact	gggtgaggtt
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43321	tcacatttct	atgtctgttc	acccttattt	ataatagtaa	tgacatcaca	aaaatttaga
43381	gctagaaatc	tagacatcaa	caaatttgat	cccaccacc	caccattat	atatactaaa
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43501	tgccactatt	atatataatc	ttatatataa	ttatatattt	gtatatataa	cttttggggt
43561	ctgaatttct	tcacattcaa	aataagtc	caagattatt	tctgagaaca	ctccaagtct
43621	aatatttgaa	tggtactact	ctaaattata	aaaagttgag	gaggccggat	gtggtggctc
43681	acgcctgtaa	tcccagcact	ttggggaggct	gaggcagggtg	gatcacttga	ggtcaggagt
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44521	actacaatct	tatggcttat	aatataacat	caacattaat	tcttaaattt	tcataaaagc
44581	atgtacatgt	taagaacata	caaagagatt	catgcattta	atgagggtgt	gaataaatta
44641	agactagtgc	attgagatta	cacagtacct	cctccaatta	gtcaggaaac	tttcttagag
44701	aaggaggaa	ttattccaag	gacagtatac	tgatagactg	actaatttta	catttccctg
44761	attgttttaa	tagcttttaag	cacaccacat	attgcagtga	gatacacaaa	ataaaaaaca
44821	aggtaaacat	ccaaactcca	aagctggcat	acgcactcgt	ttccactttt	tcactaggat
44881	aagaaggctt	agttagctat	gttttagccat	aacagaaaca	aagacagaat	gcaaaaatta
44941	gattatgttt	ttctctttta	attagaacat	acacaaggaa	tcagaaatga	aaatgccttc
45001	tctattcctc	taatcgcaaa	ctcctgacaa	atcttataat	gtaaaatagc	aaatactcta
45061	aaaaatatac	tctctaattg	tagagtttca	caaacttata	taattagaaa	actctataaa
45121	aactaataaa	gaacaaagtc	aatacaaaata	ctacaatgaa	tggtatgtta	acagaaatga
45181	tatccttagg	aaacaatctt	gacactatga	aagttttacaa	tagggaaaga	tggttcttaa
45241	ttagctacaa	aaactatgaa	acgctttgta	gcatttaggc	tagatcttgg	aggatttcta
45301	agatttggtc	acaaggaaat	gcaagaaaga	caatcaaaag	gaagagcata	agtggaaagca
45361	atgatgctag	aaagcactgg	gaataatgaa	tagtttatatt	tgactacaac	aattaaacat
45421	aagatgaact	ttactcacta	gagtatcaaa	aagaacatta	aaaaataatt	tctcagacat
45481	tatataatta	gcccacaagt	ataacgcatt	tgtttcagat	ggtggtgaca	atatccatat
45541	gaggtttaaa	atatacacat	aaaaataatt	aatcaactac	aggaagcaga	gactgaacaa
45601	aagggaattt	tcattcattc	atttaacatg	tttttataaa	aacttctctt	ttatttttga
45661	gactgagtct	cactctgtca	cctaggctag	agtgcagtgg	caccgtctcg	actcactgca
45721	acctccacct	cccagggtca	agtgtttctc	ttacctcagc	ctcccgaata	gctgggatta
45781	caggcatgtg	ccaccaagcc	cgactaattt	ttgtattttt	agtagagatg	gggtttcacc
45841	atgttggtca	ggctgggtctt	gaacctctga	tctcaagtga	tccaccgcc	tcggcctatc
45901	aaagtgctag	cattacagac	atgagccacc	gcgccagca	ataaaaaactt	cctagtatat

FIGURE 4-M

45961	tcactagcac	tctgatacct	atgatagtga	cataagggca	gcctaacata	acgattttcta
46021	aatactgcat	tgtcgggccc	gtgcgggtggc	tcaagcttgt	aatcccagca	ctttggggagg
46081	ccgaggcaga	tggatcacct	gaggtcagga	gttcgagacc	agcctgacca	acatgggggat
46141	atcccatctc	tactaaaaat	acaaatatta	gacaggcgtg	gtggcagggtg	cctgtgatcc
46201	cagctactcg	ggaggctgag	caggagaatc	tcttgaaccc	aggagggaga	ggttgcaatg
46261	agccgagatt	gcgtcactgc	actccagcct	ggaagacaga	gcgagaccct	gtctcaaaat
46321	aaatacatat	atacatacat	aaatactgca	ttgacttcag	tctttgatat	cacacagaca
46381	aaccagaagg	caatgaaaac	tgaataaact	tgtttttctt	caagtcta	ttagtatcta
46441	ttaaaaaatg	gctttgggag	tgaactcactg	actggtaaaa	aacctctct	ccttacagggt
46501	cagaaaaaat	ttcaattaaa	atttttgtta	attaaattac	ttattttctaa	gttaaatagc
46561	attaggaatc	cttatatatg	gttcatagaa	tataaaagaa	aatgtctca	aagggcagtt
46621	tcttaataac	tcacctggat	tcactttttc	gttttactgt	ttctaaaaac	aatgttgaaa
46681	aacttttttt	agcttgctcg	tgaatttcac	attctgaatc	tcgtatttcta	ttctgagatg
46741	atcctgatgg	ttttctttct	tgtccttcYg	atgtttttatc	ctcttcacatc	gatactttat
46801	tatctatttc	tattttcttt	aacataactt	tatcatcaaa	gtttaacctta	aaagggttaa
46861	aggagggtaa	gctgaatgct	cccgtaacgt	ttcttgagtt	ataagtcttc	ctgaactcct
46921	ttacagagac	aatacagacc	aattttaa	tctgtactag	gcattttattt	aagacataaa
46981	tgctgatttg	tgcatccaa	atacataaga	taaactgtctc	aggaaaatta	acttttgtat
47041	ttatcaatag	aaaaacatga	aagagaaaat	aatggctaaa	gtatacatca	atgaaatgta
47101	tagctaggca	atggttctca	gggcaatctt	agagcactgt	gacagaccaa	actttgaata
47161	tcaaagtctt	agaatatact	taactccttg	gctccagtaa	tcatacaata	ctctaaatag
47221	aaattacact	cattacagag	atctccaaat	gcaaaagacc	ttgaatccac	tttgtttctt
47281	aaaggccaaa	ggtaagggtca	agaaagagaa	accagctgtc	cacaaagcat	agcatttctca
47341	ataatactta	tgtctgtcta	ccSttgaggt	gacctgatac	acatctacac	ttgcaattac
47401	aaaaaatatt	gagaaaatac	aaattgtttc	tcttaggaag	caatcaaata	ttatcagaga
47461	gaaaacacat	tattccagac	tatagaaaag	ttaacctcta	aacttctctg	aagtacactt
47521	taagcccttc	cttaattatt	acaaactgaa	tatatgctaa	atgtatactt	tctcataaca
47581	tgtaaataat	cctccttcct	tagtgtacaa	taataataaca	agattgaatt	acattttttt
47641	aatacaaaaa	gtaaaaattt	taaagtgcgt	taacattatt	taataaaaa	gttacctttt
47701	tttggtttta	actgaaacct	ctgtacttga	aggcagcata	tttactgaat	tttcaaaagt
47761	gtaagtctct	ctcttttggg	cactagatgg	aataacattt	tgtgatacag	atgttttttg
47821	atccaaaaga	acagaagggtg	agccaacgga	taagtaaaat	tcttcatcag	cttcaactgtg
47881	atgatcattt	agtgtttctac	ttgatatttt	tttcgagtc	gggtgatttt	tggaaactaac
47941	atcaggtgcc	agaattttct	gatgaacttc	atgggcctga	actagaagaa	aattatataa
48001	agatatttgt	caattaaaag	aataataaga	gaatcaagca	ggctttttta	aaattctgca
48061	ataattta	cagaaatagt	tttcagaaaa	ctcaaagtca	ttagatttag	aatcaaagat
48121	ctatgattaa	aataagtaag	tacttaagat	tcttctatct	ttgggctaaa	aattgggtgac
48181	ctagggcagc	tagatgatat	atttacacat	acacacatgg	aatatagata	taacagatat
48241	agagagatac	aacataagca	tgtgtgtata	tatacatata	cagtatatat	gtatatgaac
48301	atztatctat	aatgagaaaa	tttaaaagaa	tgtatccata	ttctcttaac	cctcacccct
48361	cagaacgaga	tggcatttcc	ctgcttctcc	ctctaaatac	aactaacttc	cctggaaaatt
48421	atccatcaat	caacaacagg	actctgaaag	ctggaagaaa	aaaaggtaga	ctagctagga
48481	agctcaagac	cagaaacaga	caagccttag	gttttctgtc	tgtctcccat	atacccttgg
48541	actggttgc	agtataacct	gtaaccacca	ataggtgaaa	gacagggtgg	aggctgggtg
48601	gaaatgcatt	ctctgaacaa	ggtaaaccca	ccgaagacct	aatgaggaaa	ctcaagcccc
48661	attcagcact	ctcgcccatg	gagcactcct	tactacctgc	attggcaaa	caacaaagcc
48721	ctgggctgtg	ctatgggact	gtagcagtaa	aggagctcat	accaagccag	tcccgttct
48781	acaatcatag	atggcaggcg	catgacacca	catgaagctg	tagagttagt	aaacccttga
48841	ccYtcacagc	ccaaggcaac	attttgatcc	actgatagta	ttgacacccc	aggccatccc
48901	agtccctact	ttacaaccag	ggcaccagca	gacagtctaa	tctgaggcaa	gaacagcgta
48961	agagaggcca	gcaaccccct	gtcctccacc	caatgatata	aggaaaccca	ggaccagcag
49021	cttctaacca	gaaccccaca	caagtgaacc	tggaatcaa	aaggcatctt	ctacccaccc
49081	cagacagcac	caacagggaac	tgagctagaa	tcctaacagc	atcagaaaa	gaagttagaac
49141	aaaataccac	tattactctg	aacacttaac	tatcattgaa	aataaaaactc	ataaaaactag
49201	gaaagagggg	ctgggcgag	tggttcatgc	ctgcaatccc	agcacttttg	gaggccaaaa
49261	cgggtggatc	actggaggcc	aggagttcaa	gaccagcctg	gccaaacatg	cgaaccccca
49321	tctctactaa	aaatacaaaa	attagccagg	cgtagtggca	catgcctgta	atcccagcta
49381	ctcgggagcg	tgaagcatga	gaatcacttg	aacccaggag	gcggcggttg	ctcagagcta
49441	agatcacacc	actgccctcc	agcctgagcg	acagagcaag	actctgtctc	aaaaaataaa
49501	caaataaata	aataaataaa	taaataaata	aataacacag	gaaagaacct	atacattaaa
49561	ccaaaatagg	gcaactatgt	gctgtaacaa	aagattttaag	tagtctaaga	atccccctaac
49621	ataagtaacc	aaatctcagg	aatacaatga	aaacaactcg	tcataccaaa	acccaaaacaa
49681	acccaaaaaa	aaaaaaagta	agaaaataat	atcaatagac	ataaatgaga	tgaatcagat
49741	tttaaaatta	tttaacaata	aattttaaat	caaacatcat	aaaatgcttt	aataatcaat

FIGURE 4-N

49801	tacaaatcct	cttctaaca	atgaaaaaga	aactctcaaa	gtagcatttt	ttaaaaaaa
49861	gttttttgg	tattagccat	tatcagtaag	tagtgatttt	taaatattat	tttaaatatt
49921	cctaataaca	gtgatgtaa	acaaatcaaa	actacaatga	gatactacat	cacacccatt
49981	aggatgacta	ttatttataa	aaacaaaaga	taacaactgt	tgatgtagaa	aaaaatggaa
50041	cctttgtgca	tgcaactgta	gtgtgaatgt	agaatgacag	tcactatgaa	aagtgcacag
50101	tggatcctta	aaaacttaaa	actgaaagca	ggaactcaaa	gagatacttt	cacactaata
50161	ttcatagcag	cattactcac	aatagccaaa	aagcgaaaac	aacccaagtg	cccatcaaca
50221	gattaataga	taaaaagtgg	tatacacata	caatgaaata	ttacccagtc	ttagaatgaa
50281	attctgacac	atactacaac	atggatgaac	cttgaagaca	ttatgcttag	tgaaataagc
50341	cagtcacaga	taaattttct	gtctgaaatt	catggacaga	aaaaagtaga	atgggtggtg
50401	ccagggctaa	tggaaaaaga	gatactgttt	aatgggtaca	gtgtttcagt	tgtgaaaaat
50461	gaaagaagtt	ctatggattc	atgggtgtga	tagcctcaca	acaatgtgaa	tgtacttaat
50521	gctactgaac	tgtatactca	gaaataaagt	ggacaatttt	atgtttatat	tatacaatat
50581	tttaaaatc	acttctttaa	aaaagagcaa	aggaagtga	gtgtgtatat	aaacaaacta
50641	aaacaaaaag	tcttgtaaa	ttaaaaata	ttaaaatacc	tgacaacaga	aataactaac
50701	agtagtat	aagtgggaa	ttcgttgttt	cagttaccat	gtctgcataa	tataacttct
50761	taacttggct	gcataaaaca	actatttgtt	atgttcattg	attcagtaag	tcagcaattc
50821	agcagagcac	agaagggacg	gattcttcca	tgaagtctga	gccctgggat	catctgcacg
50881	cttgtttaca	catatttgac	acctgttctt	gactgcaggc	tgaggagtct	ttctctccat
50941	aatggctact	ttgggcttct	tcacagcata	ttgtctgggt	tccaagggca	actggagaga
51001	ataagaaaga	caggaagaga	gagagagaag	gagagagaga	tccagcatgc	caagcagagc
51061	catatagcct	tttatgacct	aatcatggaa	atcacatgta	ttacatatgc	cacattcaat
51121	gtatagttag	aaacaacctc	aatgaagtgg	atggggggaa	aggtgatgac	ctaagaaaga
51181	tcagaaatga	atcaaaagcc	aggtgtgtgt	gctcatgcct	gtaatccag	cactttggga
51241	ggccaaggtg	ggtggatcac	ctgaggtcag	gggttccaga	tgagcctggc	caacatgggtg
51301	aaaccccatc	tctactaaaa	atacaaaaat	tatgtgggcg	cagtgggtgtg	tgcttataat
51361	cccagctact	tgggaggtctg	agacaggaga	atcacttgaa	ctcaggaggc	ggaggttgca
51421	gtgcaccaag	attgtgcat	tgcactccag	cctgggtgat	aagggcaaaa	ttccatctca
51481	aaaaaaaaaa	aattaaaagg	aatgaatcag	ctgggcatgg	tggctcacac	ttataatccc
51541	agccctttgg	aatgctgagg	caggcggata	acttgaggtc	aggactttaa	gactggcatg
51601	gctaacaatga	tgaagcccg	tctctactaa	aaacacaaaa	aattagatga	gcgtgggtggc
51661	tgctgcctgt	aatcccagct	actcaggagg	ctgaggcagg	agaattgctt	gaacccctgga
51721	gtcagaagtt	gcagtgaagc	gagatcacgc	cactgcattt	cagccaggga	gacagaggga
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51901	ctgacactct	tttacatgta	tacagaaatg	taaaagataa	gtaaatggat	gttgaatggg
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52021	gaataatcca	cgtggtaatg	gatttagaag	agagacatca	atatgaactt	atgattactt
52081	caacatagat	acagatagtt	acatttaag	atatttatag	gtatgtgttg	atacacaagt
52141	tattgtacac	acacatacat	ttacccagct	ctatcagttg	aaaggttcta	gcagcaacaa
52201	ctctacagga	gtgacagcac	acctagcact	cagatcttgg	tttctaataa	cattaccag
52261	taaaagaaat	catgattcca	taagaaatg	gttgattctg	ggatggggca	ggagagcatc
52321	ttgtggctct	aaaaggatg	aaagtgtcca	gaaacaacaa	caaaaatggg	ccatgtcaaa
52381	gggacactgg	aaccaaagta	agagcttcta	ttagccaaat	ctgcaacaat	ctgaataaca
52441	aaataaacag	taatgaatta	taaagtagaa	aataaaattt	atccatcaag	aaaagaacaa
52501	aataaaccca	atcaagcaga	aggatgggaa	aaaataaaga	gcagaaatca	ataaaactga
52561	aaatagaaaa	ataYagaaaa	ctattgcagg	aaaaaaaaact	aYaaaatgat	aaacctctat
52621	ctaacaataa	tgacaactat	agaagacac	caaccatcaa	tatgtggaat	aaaatagggg
52681	atgatgtcac	aatagatttt	gcagccacca	aaaatagggt	aatgcttctg	tttgaaaact
52741	ggcacgagac	aaggatgcc	tctctcacca	ctcctattca	acacagtatt	ggaagtcttg
52801	gccatggcaa	tcaggcaaga	gaaagaaata	aagtgtattc	aaacaggaag	agagaagaga
52861	ggaagtcaaa	ctgtctctgt	tgcagatga	cgtgattgta	tacttagaaa	accccatcgt
52921	ttcagttcca	aaactcctta	agtcataag	taacctcagc	aaagtctcag	gatacaaaat
52981	taatggcaaa	aatcacaagc	attcctatac	accaataaca	gacaagcaga	gagccaaaac
53041	atgaatgaac	tcccattcac	aactgctaca	gagaaaataa	aatacctagg	aatacaactt
53101	acaagggacg	tgagggacct	cttgaaggag	aactactaac	cactgctcaa	ggaatgaga
53161	gaggacacaa	agagaaaaaa	attccatgct	catggatatg	aagaatcaat	aYagtgaaaa
53221	tggccacact	gtgcaaagta	atttataagt	tcaatgctac	tccatcatg	ctactattga
53281	ctttcttcac	agaactagaa	aaaactactt	taaatttcat	atagaaccaa	agagccata
53341	tagccaagac	aatcctaagc	aaaaagaaca	aagtgggaag	catcacacta	cctggcttca
53401	aactatacta	taaggctaca	gtaacaaaaa	cagcttggtg	ctggtaccaa	aacagatata
53461	tagaccaatg	gaacagaaca	gaggcctcag	aaataacacc	acacatctac	aaccgtttgc
53521	tcttcgacaa	acctgacaaa	aacaagcaat	gaggaaagga	ttctctgttt	aacaaatggg
53581	gctgggaaaa	ctggctagcc	atatgcagaa	aactgaaact	ggaccccttc	cttacacctt

FIGURE 4-O

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53641 atacaaaaat taactcaaga tgcattaaag acttaaattt aagacctaac atcataaaaa
53701 ccctagaaga aaacctaaggc aataccatttc aggacataag catgggcaaa gacttcatga
53761 ttaaaacacc aaaagcaatt Scaacaaaag ccaaaactga caaatgggat ctaattaaat
53821 gaaagagctt ctgctcagca aaagagtga caggcaacct acagaatggg agaattttt
53881 tacaacctct ccatctgaca aaggtcta atccagaatc tacaagaaac ttaaacaaat
53941 ttacaagaaa aacaaaaaca aacaatccca tcaaaaagt ggcaaatgat atgaacagac
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54061 actggtcatt agaggaatgc aaatcaaaac cacaatgaga taccatctca caccagttag
54121 aatagtgatc attaaaaaga caagaaacaa cagatgctgg caaggatgtg gagaaacagg
54181 aagactttta cactgttggt aggagtgtaa attagtcca ccattgtgga agacagtgtg
54241 gcaatgcctc aaggatctag aaccagaaat accattcaac ccagcaatcc catcactggg
54301 tatgtacca aaggattata aatcattctg ctataaagac acatgcacat ctgtgtttac
54361 tgcagcacta tttaacaatg caaagacttg gaaccaaccc aaatgcccc caatgataga
54421 ctggataaag aaaatgtgac agatatacac cacagaatac taagcagcca taaaaaagaa
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54601 catatggaca caggaggagg aacatcacac accagggcct gtggtggggg gagggaggaa
54661 aggggaaggga gagcatttag acaaacacct aactcatgtg gggcttaaaW ccaagtgcac
54721 ggggttagat gtgcagcaaa ccactttggc acagggtgtac ctatgtaaca aacctgcatg
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54901 ggaccgatac ctcaaaaaac acaaacctacc aaaaatcagt cacaatgaaa ttgataatca
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55081 caattttaca cagttccttc cagaaattag aaaaagggaat aattcccaac tcattttaata
55141 aggc aaatat taccttgata acaaaaccat acaaacacag cattaaaaaa actataaacc
55201 aatctctcct tacttaata caaaaatcct caaaatttta ccaagtcaac tccaacaatg
55261 tataaaaaat agcaatagt cacaataact gacatttata gataactaca ccaacaaca
55321 gaaaacattt tttttaaatg cccattcata aagacatgca atatcttggg tcataaaaca
55381 aatcttcata aatgtagaac tgaaattgca cagtgcatac tatgtcataa aggaatcaag
55441 atcagaaatt aataaggaaa agataatatg aaattacca acactggaaa attaacacac
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55861 aatttcccaa ccctataaaa aacatctatt aaaaacttat agctaacatc ttaatgtgaa
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56041 actagcacag ttcatgacag cctcaacctt ttgggctcaa gtgactctcc cacctcagtc
56101 tccaagtag gcaggactat aggcacatgc cactgcacaa gctaaatttt tgtgtttttt
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56281 catcactgtt atttaacata atactgaagt actagcta atagtaaga aaaggaaatt
56341 aaagacataa actaaattta ccccaacta cccacaatta ttattttaag tggcacagta
56401 ctaatttcag ttaaaatcat agaacagaca tggataccta atatcatcat tattaacaa
56461 cactgactca gagattctag caaaggcaag aagactgaaa taatcagatt aaacataaca
56521 aataaaacct ctctttagct gatgacatgg ttatatagct taaagaaaac taaaagattc
56581 aaatttttaa aggtctagaa ttaatttttt taaaaacctt ggtaagtgtc gaattaaaaa
56641 tttgatataa aaattagcct cataatttaa aaaaatgttc agaatagtac aaaaattata
56701 gtacagttag gattaacctt aacaagaaag tcaaaagccc aatactagga gggaggggag
56761 aatggggagc caggagacag gctttattaa aatatttttt atgataaaac atgaaattta
56821 caatattaac cattttatgag tgtacaattt aatggcatta agtacattca caacactgtg
56881 caaccatcat cattttctaga actttttcat catttcaaac aaattctgta cacatcaaac
56941 attaaatcac cattaccccc taccacaatc ccctgcaact tctattctgc ttcctatctc
57001 taaatttacc tattataaat acctcatgta agtagaacta caaaattttt gtcctttttt
57061 gtctgggtta tttcagtttg catgttttaa tgtgttcaag attcttctat gctattttat
57121 atagcagaac tttgttttta atgactgact aatattacat tctgtgtata aatcacatgc
57181 tgtttatcca ttcattctgt gacggacact tggcttgttt ataccttttg agtattgtga
57241 ataatactgc tacgaatat agtatacaaa tgtctgtctc catccctgct ttcaattctt
57301 ttgggtatat acctaggagg gaagtattgg gtcatatggg agttctatgt ttaacttttt
57361 gagcaactat caaattgttt tctatgggtg ctgcaccatt ttacattccc accagtgtg
57421 catgagggtt ttaatttatc cgtatcttca acacttattt tccttttttt gttttaaata

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FIGURE 4-P

57481	atagctaacc	tagtgagtgt	aaagtgggtat	ctccctaggg	tcttgatttg	cattctctaa
57541	tgactgaaga	tttcaagcat	cctttcatat	atattattggc	caattgcata	ccttcttttg
57601	agaaaagtct	atacacagaa	tgtaaagtcc	tttgctcatc	ttttattttg	gttggtttggt
57661	ttttctgttg	ttgagctgta	gaagttcttt	atatattctg	attataaatc	tctatcatcc
57721	ttttcaggta	aattattttgc	aaatattttc	gcctagtctg	gttgcccttt	cacactcttg
57781	acagtgtcct	tcagatttat	ttattttatt	atattttttt	ggagacgggg	tctcactctg
57841	tcgcccaggc	tgaggtgcag	tggcgcaatc	ttcggctcac	tgcaacctcc	agctcctagg
57901	ctcaagcgat	tctcctgact	cagcctcccg	agtacctggg	ataacaggta	cttgccacca
57961	cgctcggcaa	attttggtat	ttttagWaga	gatggagtgt	taccatgttg	gccatgctgg
58021	tctcaaatc	ctgacctcaa	ctgatccacc	tgccctagcc	tcccaaagt	ctgggattac
58081	aggcatgagc	aaccactcct	ggctccagat	taacattttt	ataagaaaga	aacataactt
58141	attttgtaaa	aaacctaaat	aacataaaaa	atgtgaattc	tcacgaaatt	actacataaa
58201	ttaaatgcaa	ttctagttag	aattccaaaa	gtttattttg	aattggataa	aactaaaagc
58261	tcatagaaag	aaaaaaggct	gcagaatggc	agtggaaatg	tgaaggattt	tatatcagga
58321	catactatga	agctactatt	agtaacaaga	gtattgtgtt	gacagaggaa	aaaacaaata
58381	tatcaaaatt	caaaagtatg	ttgaatgtta	tgtgagattt	aatatataat	aaaagtagta
58441	cattcagaag	agaacagatt	tttttttaat	tttaataaaca	gatctgacac	aactgaccac
58501	ctggaagaaa	acaaacttag	aagattatgt	catgtttacat	accgaaacac	attccMgatg
58561	gttaaagact	taattttatt	ttttaaaaat	aggttttcag	atgaaaaatc	taagttggga
58621	taagacagaa	cttttaacta	aaacaaactt	aaagctataa	aagtcacaca	tttaacaatt
58681	aaaatccaac	agccaataaa	cataaagggtg	ctcaaactct	ggcaatcatg	gaaatggaca
58741	ctaaagtaaa	aaggagattg	cttaatatca	atgaatgggc	aagaacgtag	aatagtaaat
58801	agactatcag	gtaaaaggta	ctcttacact	attgggtgta	aaggaaatta	taatagcctt
58861	ttctgaaagc	aggtagggc	acagacacat	acaaacacac	atgctttttt	ttttttcatt
58921	tatgggcacc	aattaaggta	cagaactatt	taaaggctac	ctcagcagaa	tgataggagt
58981	aatgactaaa	ttcttatatt	aaacctttat	taactcaatg	gagtaacact	cttttaactc
59041	gaaaaataaa	aagaaagaaa	actttaaaaa	gtagtagcat	gtatcactga	ctaaaggaaa
59101	tggagaagaa	gagagaaaaa	gagcactgac	catggagtgt	taaggaaWtc	aaaaacaaat
59161	tcactccattt	cacaattcac	aattctgtct	aggctgacct	tgaccttcac	actcaaagca
59221	acacatgcac	cattagcgtt	tctcattttt	taaataatc	caagcaaata	atgcccattg
59281	agatgScacc	aaactgatct	gtttgtggct	tcacttggtt	ctacaacaaa	ctgtagagag
59341	gcttctttct	tctttgaaga	aactggaact	gactttggat	gtgatttctg	gcactgagca
59401	cagaagaaat	acaacattag	aactatttta	ttacttacc	aattcaatga	aatatatttg
59461	tttttttaaat	ggggggaaaa	acaagtattc	taaaacaaca	aaccagctgt	taagatgttt
59521	atactacttt	ttatttttatt	tctaaagtaa	tagctacttt	ggaaaacaat	ctggcattat
59581	tcagtaaagc	tgaaatttca	tacaacctat	cacagaaaca	atattactct	aaacagcaac
59641	tatgtggaca	gaagactgaa	taaaacttatt	aaataaataa	attatagtat	agatatacca
59701	tattacatac	gtaacaatgg	aacaaataaa	ctacaataat	ataaattatt	atttttaacca
59761	gaaaaaaaag	caacctgcag	aagtacataa	caatcttata	tatgtaaaat	tcaaaataga
59821	cacgtaaaac	actgtagtat	tgagattcac	tctgcaggaa	agagttaaca	taggaggcct
59881	gatataattt	aaggaccagc	ttacagggtc	acccttggt	tggcatctgg	agacttaact
59941	tttagaatgt	tccctccatt	accaacagag	aaggttgcac	ctgctgcgcc	agcctgccta
60001	gactgtttgt	ataaataaac	actgtgatct	gtggtgaaca	tctgctttct	ttcctttctg
60061	gagtgcgtaa	aatttttggt	ggcaggggat	gcctatggga	ccaaccccca	gtgaaacag
60121	gctgagtttc	aaaaggcttc	tctgaggaga	aaaaatgtac	acacgttact	gcattttcaet
60181	gctgaaggga	atgagtacat	tctatatggc	cccttgRgga	acacaggaag	cctatatatg
60241	gattcctcca	gactctgcta	atgctgcatt	ttcccttact	gacccagctg	tgtatcctgg
60301	ctgaatgact	ataataagta	tcagtcatga	aaaacaccaa	aagcaatggc	aacaaaagtg
60361	aaaattgaca	aatgggactc	aattaaacta	aagagctttt	gcacagcaaa	aKaaactacc
60421	atcagagtga	acaggcaacc	tacagaatgg	aagaaaattt	ttacaatcta	cccatctgac
60481	aaagggctaa	tatccagaat	ctacaaagaa	cttaataaaa	tttacaagaa	aaaaatcaaa
60541	cagccccatc	aaaaagtggg	caaaggatata	gaacagacac	ttctcaaaag	aagacatcta
60601	tgacgccaac	ggacacatga	aaaaatgctc	atcagcactg	gccatcagag	aaatgcaaat
60661	caaaaccata	atgagacact	atttcacaat	agttagaatg	gcaatcatta	aaaagtcagg
60721	aaacaacagg	tgctggagag	gatgtggaga	aaYaggaaca	ctttttacact	gttggtggga
60781	ctgtaaacta	Kttcaaccat	tgtggaagac	agtgtggcaa	ttgctcaggg	atctagaact
60841	agaaatacca	tttgacctag	ccatcccat	actgggcata	catccaaggg	attacaaatc
60901	atgctgctat	aaagacacat	gcacacgta	gtttatttga	gcactattca	caatagcaaa
60961	gacttgcgaac	caacccaaat	gtccatcaat	gatagagtgg	attaagaaaa	tgtggcagat
61021	atacaccatg	gaatactatg	cagccataaa	aaaggatgag	ttcatgtcct	ttatagggac
61081	atggatgaag	ctggaaacca	tcattctgag	caaaactattg	cgaggacaga	aaaccaaaca
61141	tcgcatgttc	tcactcatag	atgggaattg	aacaatgaga	acacatggtc	acaggggtgg
61201	gaacatcaca	caccagggcc	tgctgggggg	tagggggagg	ggggaaggat	agcatttagga
61261	gatacaccta	atgtaaatga	cgagttaacg	ggtgcagcac	accaacatgg	cacatgtata

FIGURE 4-Q

61321	catacgtaac	aaacctgcac	gttgtgcaca	tgtaccctaa	aattttaaagt	aaaataataa
61381	tttttataaaa	agcaataaaa	aataagatc	agtcgatgag	tcaactatat	gtcaaatctc
61441	ccgagtcctt	ttagtgaagc	accaaagtgt	gatggtagtg	ggacctctgt	cacaagtggt
61501	agcagaagt	tggacacagt	atcRgcacag	tagagaaata	aataaatgac	agacttacat
61561	ggtttgcctg	tgtccccaac	caaattctca	tttgaattgt	atctcccaga	atttccctgt
61621	gttgtggaag	gcgcccagg	ggagacaatt	gaatcatcag	ggtcagtcct	tcccatgcta
61681	ttctcgtgat	agtgaataag	tctcacaaga	tctcatgggt	ttatcagggg	ttaccacttt
61741	tgcttcttcc	tcatttttct	cttgccacca	ccatggaaga	agtgcccttc	gccctatgcc
61801	atgattatga	ggcctccaag	ccatgtggaa	ctgtaagtca	aattaaacct	ccttttcttc
61861	ccagtcttag	gaatgttttt	atcagcagtg	tgaaaatgga	ctaatacact	acactgctgt
61921	tgagtgaacca	cagtatggaa	ttcaatgcc	taaaaagaca	gaggcaggct	ttcattttat
61981	ctctgctctc	tcttaacatc	tcatttaaga	tttttataaaa	caaactcaga	aggatgaaga
62041	gagagacaaa	ggagtagatg	agacatgtca	gcaaaccattt	ttaggttgaa	aagcaacta
62101	ctggtaattc	agcaaccag	agagaatgga	aacatgctag	caatggagaa	aaccagaaag
62161	cagacagatt	actgtttatg	gagaaacct	ttaaagattag	tagaattgca	agacaccact
62221	aaaaaaaagg	ggcaggccag	atgcagtggc	tcacacctgt	aatcccagca	ctttgggagg
62281	ccaaggcagg	agtatcactt	gaggtcaaga	attcaagatc	agcctgggaa	acttagcaag
62341	accacatctc	tgtgtaaaaa	taaaaaatta	gccaaagagt	gtgggtgatg	cttgtgttcc
62401	tacctactca	ggaggctgag	gcaggaggat	cacttgagcc	cagagggttg	aggttgagct
62461	gggctatgag	catgccactg	cactccagca	acagagcaag	accctgtctc	aaaaaaaaga
62521	agaggcatgc	aaacagaggg	tgYtaaaagc	gtgtatagtt	gaatgtgtct	tttgtcgcag
62581	aaaaaaaatt	gtgtatagca	agtagttaa	ctggctgggc	gcagtggctc	acacctgtaa
62641	tccccatact	ttgggaggct	gaggcggtg	gatcacctga	ggtcaggagt	tcaagaccag
62701	cctgatcaat	atggtgaaac	cttgtctcta	ctaaaaatac	aaaaattaac	caggaatggg
62761	ggcaggccacc	tgtagtccca	gctgctcgag	aggctgagac	aggagaattg	cttgaaccgc
62821	ggagRMagag	attgcagtga	gccgaaatcg	tgccacYgca	ctccagccca	ggagtgtttt
62881	ttctcaaaaa	aaagaaggta	gtaaaaccga	agagcccctc	ccaaacctat	cagaagatta
62941	tttactctct	tgagtttctt	aatcagagag	actgtgatat	tagtggcata	agacacaggt
63001	gaagttaaagg	gcaatacatg	aaaaaccag	atattaagta	ggagcattta	aactgcactt
63061	tccccctttgc	cacatctgac	tgaattgaa	aacaatcgca	gtagacttg	aaccgccaa
63121	cgggaaagat	ttctttgtca	gaaatactta	ctaggccaag	agaaaagaaa	tctacagata
63181	ttaacaccag	gataccaatg	atgaaatgga	ccaaactaca	ccacagtgc	atccaccagt
63241	ctacaaattt	tactaggcat	actagcttcc	caatgtgttt	tagtttccca	ctttcaaaaa
63301	agaggagaca	gctaaggatc	actggacata	tgaaaaaggc	gaggtaatga	gcaaatgaag
63361	taaaaaagg	acttgcagaa	aacagaaact	gaagaaataY	ttatgaaaag	ggttagatga
63421	acctaattgtc	aaggaatata	ataaaaaattt	agatcactaa	agacagatga	catgatccta
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63541	aacaggagaa	gctaataata	aggaagcaa	catttgtaag	tctaagggaa	aatacacctg
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63781	aaggagaggc	caagaaaaaa	ggaagatttc	agatccaaga	aataagagtt	gcaattcagg
63841	agaaaagcaa	aggactctc	tgtgatacag	agagagtaca	tgacaaaacc	tatgtgatag
63901	gtctaagggt	agattgaaga	aaaaaaaaag	agcagggaca	gcaaagctga	aaatgataaW
63961	ttaatgtgtc	tatgcatact	aagacattta	tacttagacg	tttgtcatag	aaaactgggtg
64021	atgaattagt	cacagggtgca	cagaaagtca	aaaatggaad	aaccaaaatt	aatcaagag
64081	aaaattaaaga	actgtacata	aagaaaattt	aaccattagt	actctacata	gctgtgacta
64141	ctgaaacagt	cataataata	ccataaacac	taactactaa	tcctactaaa	aattatgatg
64201	tactaaagaa	tggaaagtta	tgtgttgtgg	tcggaagtag	aaactatatg	acaaataaag
64261	tctaaacttc	catagtagaa	agccaataaa	taatagcaaa	gactggRaaa	aaaaatcaag
64321	aaacagcaat	ataaacatta	tttagaaata	tggagtcaaa	atacctagag	taatagctaa
64381	gactaaaaag	ttggacttgg	aggagaaaa	gtgggttcta	ctattttttt	gtggaattta
64441	tggaaactact	ttaacttcca	tgtacataat	gcctttgagc	tttaaaaatc	aatcttccaa
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64561	agactgctga	ttctttgaaa	atgttaatga	cagaaaaata	cctgtaacaa	cacagataat
64621	ttaaaaagg	gaaaaccagc	aataaaaaaga	gagtaataac	tatgagggaag	atcatgaagt
64681	tgactataca	caaattgaga	acagaggaaa	tgtttcaaga	aaattataaa	atgtcaaaac
64741	tggcaaaaga	aataataaaa	atgcaataga	tcattgaata	aagtggtaat	cacacacatc
64801	cccacaaaaa	cagctccaac	catatgtttt	acaaatgatc	caaatttgaa	gaacagatc
64861	atttttgctt	aatcaagtta	tcccagaaaa	cagaagagaa	aaactaattt	atttcatgaa
64921	gctcgttgt	gtttcagtta	aaacctacgg	agtcataatc	tatttttactt	aaagacaaac
64981	aaatatgaag	taataactag	acctaggaat	ctcaagttcg	caaacagaaa	agcctataag
65041	atagataagt	cttaagtctg	attttatttt	caaatacaagt	aaacaaaattt	cattcccttat
65101	gtggaaggcc	taggccaaagc	ttgctgcatg	gaaaggccct	acctgaaaaa	aaaaccctaa

FIGURE 4-R

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65281  aaaaacaagca aatgagagga ccgacaaagc caaacttgggt tttctgaaag accaaaattg
65341  ataaaccctg acaaaaattaa tcgatgaaaa agacaaggca tagcaggcac agtggcatgt
65401  gacttacgag cagtaatccc agctattcct tagcttaggg aggatcactt aagcccagga
65461  gttctaatacc agcttgggca acataccaag atccctacct ctaattaaaa aaaaaaaaaa
65521  aaaagataag gcataaataa ccaatgtcag gaataaaaaa ggggatataa ctgtagatcc
65581  tacagacatt aacaagactg gaaaaagaca tgacaaaaca acattatcca aataaactgg
65641  aaaattttaa taaaatgaac aaatccctaa aaaaagaaaa gtagaacatt taaaaaaaat
65701  agaaaatcta aattgtctac tgaaactRtt aagtaaaatc taaatcttta atgttctata
65761  tcatcatcta ggtagtagtt gtaaaaattc aatgaaatat acacgcaatt tgtgtatttt
65821  aatgtattat gtttcataag aaaacaaaag tgaggccagg gattgcttga gccagaagt
65881  tcccaatgct ttgggaagct gaggcaggag gattgcttga gcccagaagt ttgagacaag
65941  cctaggcaac acagttagac cctgcctctg taaagaaaaa ttttaaaatg gccgggtgcr
66001  gtggctcaca cctgtaatcc cagcactgtg ggaggccaat gcaggagtat cacttgaggt
66061  caggagttaa agaccagcct ggccaacatg gttaaaccct atctctacta aaaatacaaa
66121  tattagccag gtgtggagat gggcgctgt aaccccagct acttggggga ctgaggcagg
66181  agaatacttt gtaccccgga ggcagaggtt gcagttagcc aagatagcac cactacactc
66241  cagcatgggt cagcagacaa gactttgtct caagacagat agatagatag agaaataata
66301  aataaataaa taagcaggcc agcatggtga tatgcaccta tagtcctagg tagtcagcag
66361  gctgagacgg aagggtttga gcccaggaaa agttcaaggc ttcagagagc tgtgatcatg
66421  tcatggcact ccatcctggg cttaaagagt aaaccctgtc tcagaaaaata aataaataaa
66481  taaataaatt agtattttaa aattctcgca aagagaaaac Kcctatgaat tccatcaaat
66541  atttgagaaa gaaacaatag tggttcataa aaacacttca ggagaaaaa gacagagaaa
66601  atactgaaca actcatttta caagaccagt acaaacacag agtagaacct ttattttgaa
66661  catttcttat ttattataca tttaaagtta tgaattccct ctaacactat tttagctaaa
66721  tctcacaagt tctgataagt catattatta tcttcattca gaatatttta tattcccaac
66781  atgctttctt ctttggccta agtgcattta gaagtcattg cagtggacct tggcctttaga
66841  gcacaatgtc ttaaaaggga ccagatttac cctcctgcct gaatcaattt taaaaaaaga
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66961  gatgggaaac aaatgagggtg aaccctctga tcaccatttt ccagatgtga cacacagggg
67021  aaatcctcag ttgaggagcc aaagctgagg attcaggaag accaaagtgg ttagaatttg
67081  caggataaag tactggacag gagacggtta catagagaaa actgcagaat gtgcagatct
67141  ctctcaagca ttcaatcaaa tattgtcagc agaatgcgtt gtaagaaaac cagagaaaga
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67381  cataatccta aaatttgttt ccatttttta aaatagctgc tttagcagga gtgttagcct
67441  tctgtgactt actgcattct acctagaaga ggaacctcta gcataacctt gataccaaa
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67561  ttcaatatta ggcaaaccta atcaaaaaaa gttaatactt tatgaccaag tcaagtttat
67621  cccagaaaaa ctaaaagttgc tttaaactttc aaaaaccatt gtaatttatc aagtttcaga
67681  aggcctctca attctgaaag aaatgggtttt gtctgcattg cttggaacca aaaggctaca
67741  tatgtttaat atgttgattg ccttttacag ttttctagta agtggtactt ctgacctat
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67861  tttatttgaa agtctgctac ttagtatagt taagtcaacc aatactttat ttctgatcaa
67921  actaacagca attaaaatat ataatacaca gaagattgat ttccccgtat aacaatgaag
67981  tgccttcatt tattagaata taaccaacct tgccaacctg attagcaact ttgatcactg
68041  cccatttttc taaaaaccta atttgagtat tatttttaga gaagtgaaaa atgtttatta
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68161  ttcacaaaat acctccaaat ttaYagaaa gtcaatggga atatagaatt ccctttcaag
68221  aataagactt acaaacact cctataccag ctcttcttta tcacttacct ctttgcttgg tgactgaata
68281  aaatattaaa cctatttttg ttatttttgc tgttgaaatta ggcactgatt ttgtagaatt tgtactaaaa
68341  caagtgtctt gacctaaaac aaaagtatga aattttcaaa aacaagatat agtgtaatat
68401  tcattggcaa caattaaaag tagctgtata tgacatgtga agaaccatct gttgactcac
68461  ctattagtca tagcttaaat caagtagaga cctcaattta atattcaaat gttcctgaga
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68641  ctttcagagc tattccaata cctgctgatg ctaatcagca cttggaaaag tttttgctgt
68701  cttattctct ttccctaaac agatatgtaa atcaccaaaag attatctcaa attctccagc
68761  aatttatgac gattccaaga attctacaca tctatttttc ttatatattt tttctggcta gatgcagtgg
68821  cttatgcctg taatcccaac actttgggag gctgaagagg gcagatcact ggagggcagg
68881  agttcgagac cagactagcc aacatgggtg aacctgggtc ctactaaaaa atacaaaaat

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FIGURE 4-S

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69001 tagccaggcg tggtaggcaca cacctgtaat cccagctact tggaaggctg aggcacaaga
69061 atcacttgaa cctgggagggc aaaggttgca gtgagttgag atagcaccac tgtactacag
69121 cttgggtgac accgcaggac tatgtctcaa taaataaata aataataaaa tactttttct
69181 tgtgtatgat aattatgtat ggacttccag attacagtaa tttaatgtga actaaacggg
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69421 atctaaccct taaattccat ctgaaatga agccttactt ttttctcaa aacagtcttg
69481 taagatttcc agaacattct tgtgttaatg tgctgtgccc taataaagga
69541 aaaatacagc ctgtcatttt cagaagatat ttctttatat taccatctct ttgaaaattc
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69661 caaaacaagt acttgagggg ctatacatct cctcaagtga actctttcct tcctaataag
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69901 ctataaattc tcaaatgcat ttctaattca gtatcattga ttaatcttaa cagtttatga
69961 atcagtataa attttaatta aaaattatat tgagcttgta gattcacagc cagctatata
70021 acataataca gacccttgt tcaatttacc tagttctcct cagtgtaaat attttgcaaa
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70621 agagtggaca aacttttgct taaagggcca gatggtaaat attttaggct tgtaaaccat
70681 agtctctgtc acaaccagtc gactctccca ttctagccca aaagcaacca cagacagtat
70741 gtaaacaaag aggcattggc gtgttccaat aaaattgaaa taaaacctgt gacaaaacat
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70861 agctggaaaa gtactatata tgcagtaatt aaaaactgtg agccacagtg cattatcagg
70921 tcatccatca taaagtttta taactgaaag atctcagaaa tcatccagtc caataatcat
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71221 tttctaccag aatatatata ggtgactatt ataaaattctg gccttgacat caccocaaaa
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71341 aaggatgaga tccaaaaaga tcagatttgc caaggtgata atgcagagtc actattagaa
71401 cgcaggtcac attaggcaac agctttttca aaatttatca aattcgtctt ttcttccctc
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72181 cctattacta gtaaatattt aactagaaaa ttacttttt acaggtttta caactaaaag
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72661 tttttgagat gatcctgaaa gaaaagttaa tcatcaattt ggtttcttta agatagagtc
72721 gagtaaaatt tattttcaaa gtaacttcat ccagtatggg catgctatac accaaacatc
72781 tcctaagggc tcaaaacaat tttgaggtta tgttatgaca taacataggt tatgacaggc

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FIGURE 4-T

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73081 aatgatacgg atttttatat agtaaccata accaaagtat gaaatataga atagtgaaca
73141 ccaaagaagt ccagaaatat gtaaacaaaa tgagttgtcg cccccattag tcattcacag
73201 cttgtacctt ttaactgata gctgtctttc agaagagttt gtcaataaca tatgctccat
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73321 aattatttcg agacgtactt gttacataat ctgtttctcc caactaccaa gtgtgacgca
73381 aagacacact tttaaggcgt ttcaatactt ctaccatggg gagaaaagtt atttgaggc
73441 ctaggaactg gagctagact aaaaagcaga agccaagatc gcgccactgc actccagcct
73501 gggggacaga gcaagacccc gtctcaaaaa caaaaacaaa aaaaaaccca gcagaaatca
73561 caagcacctc tcaagagtaa gacgtaggca cagacgaaat gacgacatga aaacttaaga
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73681 aaattcctgc ggctttccca ctgaaatccc tcagagatca cagcctcagc ctagcatttc
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76561 ctatatctat ttgtcaaaat tcctagttag aactgtgccc ctgaaaaagg cgaccttttt
76621 ttttttgaga aaggtcttgc ttggttgccc aggctggagt gcagtggcac aatcaaggcc

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FIGURE 4-U

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76681 cactgcagcc tctacctgct gggctaaaat gattctcctg cctcagcctc gtgaatatct
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77341 acaatactct ttcagtttct ctgtatgttt gaaatatttc atagaaaaat gatggggaaa
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80461 ttgggaagct gacattaatg cttatgtctc caagatcata ctgacatcat gcaatcagga

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FIGURE 4-V

80521	agccaccaca	attacaaagc	tgccacgtta	tggaaatcac	tataagaatt	aaagaaagag
80581	gaaagaaaca	caaaaagtgg	cttgacagcc	aaagacaggt	ttatttttaga	gaaaccccaa
80641	gggggcttct	ggccaagtta	ggtcagagcc	acactctctt	acagactaag	agttttttaag
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81001	ctttctggct	gctttagtgg	agaagagaag	tgatttcctt	gaaatgcatg	aggctaaaaa
81061	gggagctgga	acttaaagtg	gcagtatatt	agatgatggg	gctcctgctc	tgtcagtcac
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81781	atgatgatata	gcacaagcaa	actgatgtct	gtgacttgac	tatcaacacc	catgaagcta
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81961	gttaattcca	gctactcaga	aggctgagcc	aggacgattg	cttaagccca	ggagttttag
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83221	cattgataag	ctataagtat	ttcacacaat	ggttaaaatt	aaagttgtat	tcttcaggta
83281	tgagttgcaa	aaataaatgt	attcaattaa	aatatcttag	aaatatacta	ccgcaaatta
83341	taatgcatat	ggcaataaat	catcagtaag	tattaagcaa	aacaaaggtc	agaaatgtgg
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83461	tatttttagag	atcctcaatt	attgtaaaaa	atgtggattt	ttactcagat	gaccttataa
83521	catagaggag	tcaatacagc	actgagattt	tggtttatat	gagttaaatc	ttatacttca
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83641	agatgctact	gatggctgta	atgttgggct	ccaatagttt	aatagtaaca	tgattgttct
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83881	tttccttttg	aaaaactgtt	tctgtttgat	actcaatgta	tacaaataac	tacaacagga
83941	caaatactat	aagaaagaaa	tcgtgcaagc	tgctttggga	aagcagaaat	gagagtaata
84001	actttttttt	ttgtgggggt	gaagaaagct	tcaggaaatt	aggagatggt	cagaattaaag
84061	gatagattca	gcctgggtct	tgaaggacga	gtaggacatt	accataataa	caaagagaag
84121	gaggggcatc	taagcagagt	acagtgactg	aaaaggtagt	aggagacagg	gaagatcata
84181	gggtattcag	gcaactgaga	ctaaatgaaa	ttaccagagc	aaagggtatt	ttgaggagtt
84241	attattttaa	agggggccctg	ctataaagga	ccaacgtgcc	atgcttgagc	ccattgttgg
84301	tattcaataa	gtatttagtg	ttcaataaaa	aatattttaa	aaggaatctc	aaaagcaatg

FIGURE 4-W

84361	agaatccttt	aaagtctttt	cagtagggga	atatcttgat	taggttgaat	attaaatgaa
84421	tcaaagaaga	aaaagagtgg	aaactaggag	actacttaaa	agccttttgc	agctcttcaa
84481	acaataagtc	atgtagtcca	tcgcctcctt	gtatagggtga	ggaagctatg	ataccagaga
84541	agtcaagtgg	tttgttcaag	gtotcaagag	ctgggttagta	gcaaaattag	tttatgccct
84601	atgtccaaac	atatttttcta	ctatatttcc	ttacctacaa	atttattcctt	cactgcctaa
84661	gacttgaggt	atctgtgaaga	ggattttccat	tgtaatgggtg	cagtgggtgca	atgacactag
84721	tcattgcaga	caggactaac	ttgttaatat	tgtttaagca	agatttttgc	attttgtagt
84781	ctttttcagg	gagatataat	ttgattcttg	gtatattaag	aatgaatttg	acgaacaaat
84841	cagcagacca	aagtaactta	ctgtgtctga	ttagctgttt	ttaaattggt	gcttatattt
84901	taaaggcaaa	aaaaaaacta	agtgtcttatt	taacaacaac	aaaaaatccc	ctttacattt
84961	tttttagaggt	attattttct	ctcacctatg	aaactttctg	accataaagt	cagtgcgtaa
85021	tcactgatga	ttcccagcat	tctttcttta	tccttgcttc	ttttcatttt	tcaattctta
85081	atccctcctt	tcacttcccc	cctgtattac	aacaactaac	agctgccaa	aaagtggatt
85141	aggctcatata	ttcaatcagg	aggttttcct	gttattcaag	tcacttttct	agtataccga
85201	aactaaaaaa	tagttatggt	ttttgcctca	aaaaattcag	ttggacttat	attttattat
85261	ttgaagggttg	ggtagcaaga	agcaggtcta	aacttacaaa	agcaaagcag	tcattttgga
85321	tcttcaactc	cctattttctg	tcttgagctg	ttttcatttt	gataatacat	ctgaacactc
85381	ttctctaact	tactgataat	cagtcctgat	tgttctacct	cactttgtag	acaatttgtc
85441	atcccatatc	tacagctgca	ggatcagttg	gaccataact	gggtggagaaa	accatgcagt
85501	ctctccatta	ggaaaggaga	atcagactga	agactcctga	cttgctttga	tttctaataa
85561	taggctgggtc	tcactgggcc	caggctgttc	taaatctaga	gtagttctga	aatactgagt
85621	gtgaaatagg	caatggtaga	aattcttagg	acccctgtaa	gacaaatcaa	aattccttct
85681	agtattcttt	tctcccatca	ttctctgcac	tgYgtacgc	caaatccaat	ctcttaagga
85741	ccatttctcta	catgcaacca	ttgagtgcac	tttggtccca	gtatagcttt	ataaatctca
85801	ctagataact	gtgggaagtc	catccatgaa	tcatagtatc	aatgggtctgc	agctcagaaa
85861	gcacaaaaga	acaaaataaa	agtttgaaaa	cttacagctt	tctctgccag	atattttttt
85921	gccaaatata	ttagactcct	ttgtgttgct	gtaacagaat	gccacagact	ggtaatttat
85981	aatgaacaga	aatgtatttc	gctcatgggt	ctggagtctg	gaagtcaaag	aacatggcca
86041	gcatctgatg	aggaccttca	tgacagatca	ttccatggca	gaagatagaa	gagcaagaga
86101	ggatgatagc	atgtgagaaa	gtgccaaact	tgattttata	aaaaaccac	ttccaggcca
86161	ggtgcaatgg	ctcacacatg	taatcccagc	actttgggag	gccacagcag	gagaatcgct
86221	tgagcccaag	agtttgagac	caacctgggc	aacataggga	gatactgtct	atacaaaaaa
86281	tgaaaaggtt	agctaggagt	gggtggcgct	gcctttagtg	cccagctact	taggaggctg
86341	atgtgtgagg	attgtttgag	cctgaggagt	caaggctgca	gtgagctgtg	attgcaccag
86401	tgtattccag	cctgggcaac	agagcaagac	cctgcctctg	aaaaaagaga	aagaaaccac
86461	ctcccacagc	attaattaat	tcattcattc	atgagggcag	aggcctcatg	acttaatcac
86521	cttctaaga	tcccatttct	aaacactggt	gcattgggga	ttaagtttct	aacacataag
86581	ttttggagga	cacattcaaa	acatagcact	aaatattcat	tgggaaactca	tgtacttggg
86641	atatctactg	gcaaaaaaaa	aaaaaaaga	aagaaagaaa	aaagaaaaaa	attccatatt
86701	ccgtgttccc	ataattgtgg	tttatattta	gtgaagcatc	aaatgagcat	gagatacaac
86761	tatttttttt	atttacacaa	aacttgaccc	taaaatattt	aaccaacaga	agtagtacta
86821	ataaaattat	tctatgaagt	aatttttaat	gaagctgagt	ttattcaagt	caYgtcttct
86881	gcaaatataa	atggacacca	ataaacaaaa	acaaagatag	aagaataaac	tgtgttcttg
86941	atatctcccc	taaagttcac	aatctctaca	cctgtttctt	tcattctctg	gtgatgttaa
87001	tcttctgttt	attttgcgct	ttaaatctaa	gcacatgtgg	attaccacaga	gattgccctc
87061	tgaaagtcag	tctacacctg	ttctttctta	cctcacaaaa	agtaatggaa	aaaaaagtgt
87121	gtgtgtgtgt	gtgtgctgtc	gtgtgtgtgt	gtgtcctgtt	gggtggtagt	ttggtggtta
87181	aaaagcaatt	tgggacttcc	tctttgaaca	gttgcccttt	cctctcacag	aaggaagatt
87241	tcatttttgtt	tgagacgaga	aaccacaaac	cacaccaaag	agagggttat	gatggctaag
87301	aagcccccaa	aaccagcccc	tcgcaggatc	ttccaggaaa	ggttaaagat	tactgctcta
87361	cctttgtact	ttgaagggtt	tttattaatc	aagcgggtcag	gataccgggt	gagtctatag
87421	atgataatgt	taaaccctaag	acttctgttt	taatttaata	tttatttcat	ggtgatgtga
87481	tgtgttaaga	octocttggt	tctgttgaaa	ttaaatcatc	ttctcttctt	tgagctcaga
87541	aaaatgattc	caatttttca	taatttaaat	acaatgtctg	gcttaaacct	gtatgtatac
87601	acatatataa	tatgtataat	aacagagggt	gtaatatata	ggcactaata	taaaaaagtc
87661	aataagctaa	atttccaaag	aattttattta	aatatcacaa	aagatttttg	cttgggagat
87721	aaaatgtttc	ttgtattttc	tccacaattt	attgctatgc	ttcaatgatg	acatgtacca
87781	tttaagataaa	atgatatcat	gattaaaatt	aaacctgtct	ctgttctgag	tcatttgaag
87841	tttataatga	tcaaattatt	aaaaatggct	tttgtaaaaa	ttgttaaaat	gacaaagttc
87901	atactgttta	acattatata	tagttatgtg	ttctaaaaata	ctattcaaga	tagtgacttt
87961	taatttttgg	ggtactactg	tgggtatttaa	gtacactaag	ctacataaat	acctttgctc
88021	taagaaaatc	catgaagcat	tctgtatttt	taaatgtaat	aattaaaact	tatagttagt
88081	taaaatcatt	acttttaaaa	cagtaatttat	ggatgacttg	aaattaatta	gagaaataag
88141	cccaaaattg	cctgtttatta	aataaaaaaa	tcattaagtt	aggtcaaaat	ttatgaaatt

FIGURE 4-X

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88201 gtatactgac taaaactaga aaaatttttaa ggtttttcaga aattccatca gaaatgttta
88261 atgatgctaa aatatatttt ctgaggattt atgaatactt gtggaaaaat tatatatatg
88321 aaaaatctat aatagcatat tcacatttct tacatatata atcagatcat ttactatttg
88381 agagtaaaga catggtaatt tgtattctgt tatggatgtt aaacatgcat aaataattac
88441 ctttcagtta tattagaatt ttttagattg atcctatatg cttttaatgt aaattcaatc
88501 ttgtcaccac aggtaagcca catagtcaca ctttgccagg aaaggggaagt tgagaaaaaa
88561 aaattctaatt tagtaattta aatcaggttg ttcattgaat gttttccaag gtatttataa
88621 taactgttta tgatagcagt tttttttaa tgcttaaaga agacatgtca ttgggatggg
88681 tagcagaaag aataagaatt ttagagtgtc ctttatctga tggttttgcc acttatagct
88741 tgtgatcttg tgcaagttac tcaatctcct tgagactgtt tcaactataa gatagagagt
88801 atactacttg ctacttgctt cctaaggtag attctaggat tcagtaggtg ttcaatcaat
88861 ttattcactc aacatttatt gtgtgcctcc tatgcaccaa gcatcactca tttctggaga
88921 atatggaaaa aaacacaaag attttatttt caagaggctt aatatagtag gaatgatgtc
88981 ttctttacca aatttctact ctttaccttc tcttagaaag cattctttga agcagaatga
89041 atacctatag gcataaatat ttccaatgaa attaacttgt gtttctattt gaatttatag
89101 taaagtatct ttgtgtgtgt ggggtgtgtgt ctgtgtgtgt gtgtgtgtgt gtgacagtgt
89161 ctctctgtgt gcccaagctg gagggtcaatg gtgcaatcac tagtcatgca gccttgacat
89221 ccccggtctc ggtgattctc ctgctcagc ctctctgagta gctgggacta caagcgcata
89281 ccacaccggg ctaacgtttg tattgtttat agagacaggg tttcatcacg ttgttcagggt
89341 tgggtctcaa ctctggggt caagcaacct gccaccttg gcctcccaat gtgctagaat
89401 tacaggcatg ggcctctgag ttagaccact aagtaccttt tacttgtagt tcagggagaa
89461 gagagcaaga ggatgacaat aatacctact tatgtggtgg tttcagggat taaagggata
89521 gcatagttaa aacacctggc tcacactaaa ggttagattc attctcttac cctttcatca
89581 cttatcatat tcttattcag gtactaaaa tagtttgagg tctgcaagta atatgactcc
89641 aaggagagtg agcatggtga taattagagt acttgaatat agaagctatg agaaaaatct
89701 aagcaaaata agtggaaatt ccaagcaatt ggcagcaaag tgccagggaa tctttgaaca
89761 gaagggtgagc caaagggtata tagccaagta atctttggag ctgattggct agaggaaggt
89821 gagaggctct gcagaatgta aagttgggtc tctgccaaag tcattcagaa catttaaact
89881 agaaaaataa tcttagaaga gtaactgggt ctataaaggc atgaaatgct gagagggtct
89941 tcttagctat tttttgtggg gcacttttaa gtatttaaag agcttttccc caggaaaatg
90001 taacaacgta taccattttg catgcaattc tagaaggttt ctaaactctga ggtcaagaac
90061 ccatgaaaaa cacataatct ttatggaaaa gataatgtgg gaagatttat ttaagccaca
90121 gcactaggat tctgaattaa ccaggaagat gtgtttatta tcaaagctgt taaatgccac
90181 agtggaaatac cattggcatc gcagttctta caaatgggaa aatttctcat ttttctggg
90241 accgtttgaa aataagagag agtgtgggtg ggccgggagc ggtgggtcat gcMtgtaatc
90301 ccagcactct gggaggccca ggtgggcgga tcacgaggtc aggaaatgga gaccaacctg
90361 ttcaacatgg cgaaaccccg tctctactaa aaatacaaaa attagcaggg catggtggca
90421 cgcactgtg gtcccagcta ctcgggagc tgaggcagga gaatcacttg aacctgggag
90481 tcagagggtg cagtgatccg agatcgccgc actgactcc agcctggcaa tagagcgaga
90541 ctctgtcaaa aaaaaaaaaa aaaaaaaaaa gaaagaaaga gagaaagaa gaaaagaaaa
90601 agaaagaaaa taagagatag tttgggcaac gtctcataat ttcttcaatc tgtgatgtgc
90661 taaagtaaaa aaaaaaaaaa gtgtgtgtgg gccgggcccc gtcccagcta ttcggaaggc
90721 tgaggcagga gaatcgcttg aatctgggag gcggagggtg cagtgaagtc agatcggtcc
90781 actgcactcc agcctgggtg acagagcgaa actccgtctc aaaaaaaaag gaaatttttt
90841 agggctgtct aagttgtgct cacacacagt tctctatggc agtaatctcc aaatttttaa
90901 ataacacact cttttcagga aaacattttg agcacagatc cctaataata gaataattaat
90961 tcagccgggc gtggtggctc acgctgttaa tcccagcact ttgggaggcc gaggcgggcg
91021 gatcacgagg tcagaagatt gagacctacc tggctaacaa ggtgaaaccc tgtctctact
91081 aaaaaaaaaa aaaaaaaaaa attagccggg cgagggtgtg ggccctgta gtcccaacta
91141 ctcaggaggc tgaagcagga gaatggcggt aacccaggag gcggagcttg caggggagcg
91201 agattgcgcc attgcactcc aacctgggca acagagggag actccatctc aaaaacaaca
91261 aaaaaagaat attaatcat ttggaaatta taaatatata tattcccgta ctattaatcc
91321 atgtaaatat tttgatatat aaaaaatgaa ttaagaaata tgaaataaaa tataattaaa
91381 tattctaaaa ttttctctcc caatggatca tcttgacac ctttggaaat tatgcatccc
91441 attttgagga ccactatata acattcttcc ttaggtaaat gtactttact tgcgcacaaa
91501 aacaaagaat gagagctttt tattggggac agaggaagag aaacttaact ggagcttgca
91561 ttgtaattca tttttgctag ttaattcatt tttgctagtt gtattaatga gaaaagagca
91621 ctgggaagtc aagagataaa agtatacgt caattctaga atttgggcga ttcttccaca
91681 tttttaaatc tgttctctcc tttctaaaaa gaataattac tctcttgcat agctgaatag
91741 gttgctccaa tgactaagtg gactatataa taatgaatgc aaccttttga ggtataacat
91801 ataatggatM ccattctagg ctcttagtgt tctgtcactg tgatccttac agtaactctt
91861 ctgggtagaa attattttat tcacttcaca aatgagtgag taggtgaggc atgctggctc
91921 atccctgtaa tcccagcact tatggaggcc aaggcaggag gattgcttga ggccaggagt
91981 tggagatcag cctaggcaat atagcgaaac cccatttcta caaatcaaa aaattagcca

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FIGURE 4-Y

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92041  ggcggtggtgg cacaccctgt attctcaggt actcgggagg ctgaagtggg aggatcactt
92101  gaaccagga gttcgaggct gcagtgagct atgattgcat cactgcaccc cagcctgagc
92161  aacagagcga gaccctgtct ctctaaaaca acaactccaa ataaacaaat gagtgaagttc
92221  tggccacaga ggttattcaa ggttcctcct ccattaagga ggctagcttg gatttgattg
92281  tgatgcactt gaccatgctg cttctcaaac tcaaattcta ccatttgatt gtaggtttcc
92341  tagttaagct agtgataaat tcagaagtct tatttcagcc tcttttctta catcaatgat
92401  ttcacacaaa cgattgttaa aaaaaaaaaa aaagaaattt gtgcttcatt ccaaagatat
92461  gtccttccaa attaatTTTT ttaattttta agtatttctc tagatatgaa taggtacctt
92521  gatgttggtt attgagattg atattttata atgactcaga ttctatgtgt atttattaca
92581  tcttatcgaa atgaaatcaa gattgtgaYc tgtaagtctc tgcatactga atataagttt
92641  ggtctgtcct taggtttgca gctgtggttg cagttcacat ggtctaatagc tatttgtaac
92701  cttacttttc ctccagggct gcctttgctt tcaacttagt gcctttatac ttgcttttcc
92761  ccccatTTaa taaatcctta atcctttcca caagtatata cgtttgctta cctgtaaaac
92821  tcccatTTTT ccctatttaa ctttacccaa ttcatatcat tcttttgaga ctgaacacct
92881  ctaYaatttt tctcgatagt gcaatggagg tctgcatgta catacagagg gaattcaata
92941  aacctttact ggctatcagt aatactagtt tttatacctt atggcagggt aatactgtag

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FIGURE 5

NM_004087 [gi:4758161] Homo sapiens discs, large homolog 1 (Drosophila)
(DLG1), mRNA

Gttggaaacggcactgctgagtgaaggttgaggggtgtctcggtatgtgcgccttggatctggtgtaggcgaggtcac
gcctctcttcagacagccccgagccttcccggcctggcgcggttaggttcggaactgcgggacgcccgggtgggctagggc
aaggtgtgtgccctcttctgattctggagaaaaatgccgggtccggaagcaagatacccagagagcattgcaccttt
tggaggaatatcggtcaaaactaagccaaactgaagacagacagctcagaagttccatagaacgggttattaacata
tttcagagcaacctctttcaggctttaatagatattcaagaattttatgaagtgccttactggataatccaaatc
tatagatcggtcaaagcgtctgaaccaattcaacctgtgaatacttgggagatttccagccttccaagctctactc
tgacttcagagacactgccaaagcagccttagccctagtgtagagaaatacaggtatcaggatgaagatacacctcct
caagagcatatttccccacaaatcacaaatgaagtgataggtccagaattggttcatgtctcagagaagaacttatc
agagattgagaatgtccatggatttgtttctcattctcatatttccaataaagccaacagaagctgttcttccct
ctcctcccactgtccctgtgatccctgtcctgccagtcctgtcgtgagaatactgtcatcctaccaccataccacag
gcaaatcctccccagctactggtcaacacagatagcttggaaacaccaacttacgttaatggcacagatgcagatta
tgaatatgaagaaatcacacttgaaaggggaaattcagggcttgggttccagcattgcaggaggtacggacaacccac
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cttgggttcaacattgtaggaggagaagatggagaaggaatatatttcttcttcttagccggaggacctgctga
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aggcagcagctgcattgaaaaatgctggccaggctgtcacaattgttgacaaatcgcacctgaagaatacagtcgt
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gactgaacttcaaatttggagatatcctccatgttattaatgcttctgatgatgaatggtggcaagccaggcaggtt
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agttaattatactcgaccagtgatcatattgggacctatgaaagacaggataaatgatgacttgatctcagaatttc
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tctatatggaacaagtgttcagttctgtacgagaagtagcaggaaagggcaaacactgtatccttgatgtgtctggaa
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atggaaatgaataagcgtctaacagaagaacaagccagaaaaacatttgagagagccatgaaactggaacaggagtt
tactgaacattttcacagctattgtacagggggatagctggaagacatttacaaccaagtgaacagatcatagaag
aacaatctggttcttacatctgggttccggcaaaaagaaaagctatgaaaactcatgtttctctgtttctctttcca
caattccattttcttggcatctctttgcccttctctctggaaaaaa

FIGURE 6

NM_014660 [gi:7662303] Homo sapiens PHD finger protein 14 (PHF14), mRNA

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ctgaggcagccgccctcgcgctgtgcaatttctgggtctttcggttgccttctggtccaggctaataaagtttttctttc
tttaatttttttttcttctagttttaacgggagaaaattaactccccggggccgcccgggttgactgcgctgcctgggc
ggaggtcttctccggccaggagcgctgtgggaaggggctcgagcggccaggccaggcgagggccggggggggcgggg
ggttaggggaccgcggggctactcttgggagcgccccctgtccggctggtgcgcccgggttttaaatagcatctttc
ggaacttgctcttcgcgcccccagtcccccgacctcgcgctgcctgggctcctgcagcctctccctaagtcttctcca
acgaccacctcacggattccttatggatcgagctccaagaggaggcaggtgaagcctttggcagcttctctgctgc
aagctcttgattatgatagttcagatgacagtgatttttaagttggagatgcctcagattctgaagggagtggtaat
ggaagtgaagatgcttcaaaggacagtgaggaaggttccctgtagtgattctgaagaaaatattttagaagaagaact
gaatgaagatattaaagtaaaagaagaacaacttaaaaattctgcagaggaagaagtactatcatcagaaaaacaat
taattaaaatggaaaaagaaggaagaagaagaaaatggagaaagacctaagaagaaaagggagaaagagaaggaaaa
gaaaaggaaaaggagaaagagaaggaaagagagaaggaaaaagcaacagtatctgagaatgtggctgcttc
tgctgctgccaccacaccagccacaagtccctcctgctgttaacacatccccttctgttcccactacgacaaccgcta
cagaggaacaagtgcgagcgagccaaaaaatggaacctgcagcaaacgcaccacttctggattttgtgtccatggaa
gagctgaatgacatggatgactatgacagtgaggatgacaatgattggcgacctactgtagtaagagaaaaaggag
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agaatgatgaaggcaatgatgaagatcatagtagccctgccagtgaaagggggttgaagaagaagaagagtaaggtt
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```

FIGURE 7

NM_012074 [gi:13442997] Homo sapiens D4, zinc and double PHD fingers, family 3 (DPF3), mRNA

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FIGURE 8

NM_001812 [gi:4502778] *Homo sapiens centromere protein C 1 (CENPC1), mRNA*

```

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FIGURE 9

NP_004078 [gi:4758162] synapse-associated protein 97; discs large homolog 1; presynaptic protein SAP97

MPVRKQDTQRALHLLLEYRSKLSQTEDRQLRSSIERVINIFQSNLFQALIDIQEF
 YEVTLLDNPCKIDRSKPSEPIQPVNTWEISSLPSTVTSETLPSSLSPSVEKYRY
 QDEDTTPQEHISPQITNEVIGPELVHVSEKNLSEIENVHGFVSHSHISPIKPTEAV
 LPSPTVPVIPVLPVPAENTVILPTIPQANPPPVLVNTDSLETPTYVNGTDADYE
 YEEITLARGNSGLGFSIAGGTDNPHIGDDSSIFITKIITGGAAAQDGRLRVND
 CI LQVNEVDVRDVTHSKAVEALKEAGSIVRLYVKRRKPVSEKIMEIKLIKGP
 KG LGFSIAGGVGNQHHPGDNSIYVTKIIEGGAHKGDKLQIGDKLLAVNNVC
 LEE VTHEEAVTALKNTSDFVYLKVAKPTSMYMNDGYAPPDITNSSSQPV
 DNHVSP SSFLGQTPASPARYSPVSKAVLGDDEITREPRKVVLHRGSTGLG
 FNIVGGEDG EGIFISFILAGGPADLSGELRKGDRIISVNSVDLRAASHEQ
 AAAALKNAGQAVT IVAQYRPEEYSRFEAKIHDLREQMMNSSISSGSGSL
 RTSQKRSLYVRALFDYD KTKDSGLPSQGLNFKFGDILHVINASDDEW
 WQARQVTPDGESDEVGVIPSKR RVEKKERARLKTVKFNSKTRDKGQ
 SFNDKRKKNLFSRKFPFYKNKDQSEQET SDADQHVTSNASDSESYR
 GQEEYVLSYEPVNQQEVNYTRPVIILGPMKDRIN DDLISEFPDKFGS
 CVPHTTRPKRDYEVDGRDYHFVTSREQMEKDIQEHKFIEA GQYNNH
 LYGTSVQSVREVAGKGKHCILDVSGNAIKRLQIAQLYPISIFIKPKS
 MENIMEMNKRLTEEQARKTFERAMKLEQEFTEHFTAIVQGD
 TLEDIYNQVKQ IIEEQSGSYIWVPAKEKL

DLG1 Domains

Gene	Prediction Method	Accession ID	Domain Description	Start	End
DLG1	Pfam	PF00595	PDZ	218	304
DLG1	Pfam	PF00595	PDZ	313	399
DLG1	Pfam	PF00595	PDZ	460	540
DLG1	Pfam	PF00018	SH3	578	644
DLG1	Pfam	PF00625	Guanylate_kin	741	843
DLG1	prosite	PS00856	Guanylate_kin	740	757
DLG1	pfscan	PS50106	PDZ	218	256

FIGURE 10

NP_055475 [gi:7662304] PHD finger protein 14 [Homo sapiens]

MDRSSKRRQVKPLAASLLEALDYDSSDDSDFKVGDASDSESGNGSGEDASKD
SGEGSCSDSEENILEEELNEDIKVKEEQLKNSAEEVLSSEKQLIKMEKKEEEE
NGERPRKKREKEKEKEKEKEKEKEKEKEKEKATVSENVAAASAAATTPATSP
AVNTSPSVPTTTTATEEQVSEPKKWNLRRNRPLLDVFSMEELNDMDDYDSED
DNDWRPTVVKRKGRSASQKEGSDGDNEDDEDEGSGSDEDEDEGNDHSS
PASEGGCKKKKSKVLSRNSADDEELTNDSTLSQSKSNEDSLILEKSQNWSSQ
KMDHILICCVCLGDNSEDADDEIIQCDNCGITVHEGCGYGVDSIMSSASENS
TEPWFCDAKCGVSPSCCLCPNQDGIFKETDAGRWWHIVCALYVPGVAFGDI
DKLRPVTLEMNYSKYGAKECSFCEDPRFARTGVCISCDAGMCRA YFHVTC
QKEGLLSEAAAEEDIADPFFAYCKQHADRDLDRKWKRKNYLALQSYCKMSLQ
EREKQLSPEAQARINARLQQYRAKAELARSTRPQAWVPREKLPRPLTSSASAI
RKLMRKAELMGISTDIFPVDNSDTSSSVDGRRKHKQPALTADFNYYFERNM
RMIQIQENMAEQKNIKDKLENEQEKLHVEYNKLCESLEELQNLNGKLRSEGQ
GIWALLGRITGQKLNIPAILRAPKERKPSKKEGGTQKTSTLPAVLYSCGICKKN
HDQHLLLLCDTCKLHYHLGCLDPPLTRMPRKTKN SYWQCSECDQAGSSDME
ADMAMETLPDGTKRSRRQIKEPVKFVPQDVPPEPKKIPRNTRTRGRKRSFVP
EEEKHEERVPRERRQRQSVLQKKPKAEDLRTECATCKGTGDNENLVRYPS

FIGURE 11

NP_036206 [gi:13442998] cer-d4 (mouse) homolog; 2810403B03Rik [Homo sapiens].

MATVIHNPLKALGDQFYKEAIEHCRSYNSRLSAERSVRLPFLDSQTGVAQNN
CYIWMEKRHRGPGGLAPGQLYTYPARCWRKKRRLHPPEDPKLRLLEIKPEVEL
PLKKDGFTSESTTLEALLRGEGVEKKVDAREEEESIQEIQRVLENDENVEEGNE
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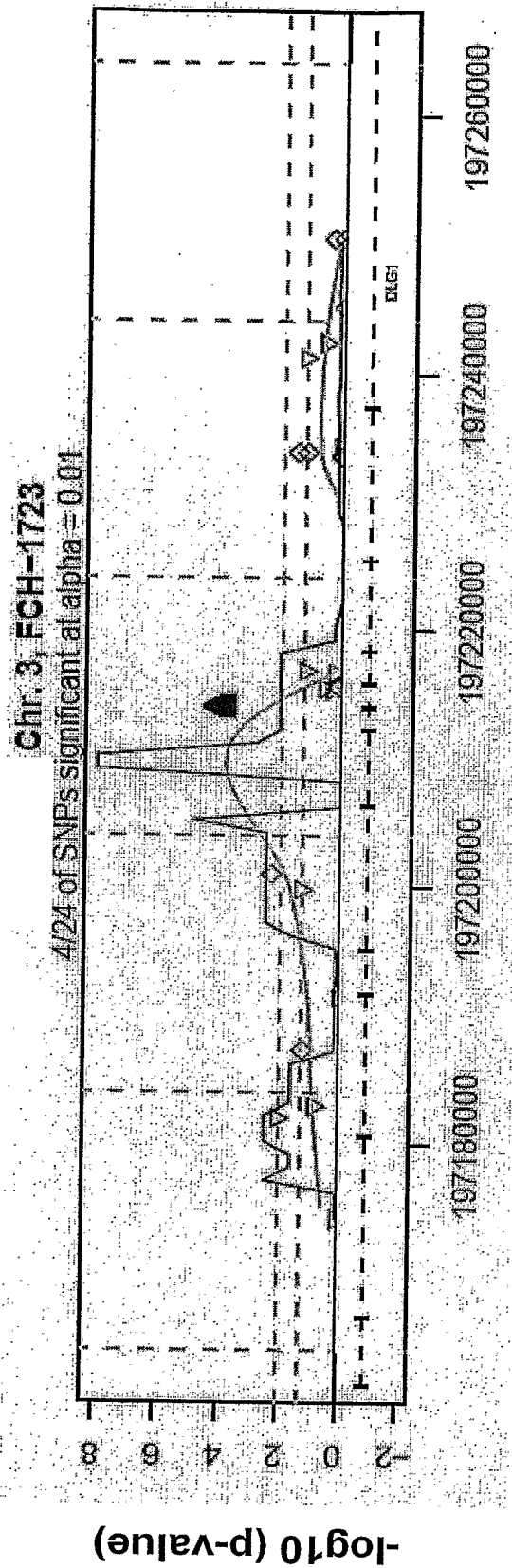
FIGURE 12

NP_001803 [gi:4502779] centromere protein C 1; Centromere autoantigen
C1 [Homo sapiens]

MAASGLDHLKNGYRRRFCRPSRARDINTEQGQNVLEILQDCFEEEKSLANDFS
TNSTKSVPNSTRKIKDTCIQSPSKECQKSHPKSVPVSSKKKEASLQFVVEPSEA
TNRSVQAHEVHQILATDVSSKNTPDSKKISSRNINDHHSEADEEFYLSVGSPS
VLLDAKTSVSQNVIPSSAKKRETYTFENSVNMLPSSTEVSVKTKKRLNFDDKV
MLKKIEIDNKVSDEEDKTSEGQERKPSGSSQNRIRDSEYEIQRQAKKSFSTLFL
ETVKRKSESSPIVRHAATAPPHSCPPDDTKLIEDEFIIDESDQSFASRSWITIPRK
AGSLKQRTISPAESTALFQGRKSREKHHNILPKTLANDKHSHKPHPVETSQPS
DKTVLDTSYALIDETVNNYRSTKYEMYSKNAEKPSRSKRTIKQKQRRKFMAK
PAEEQLDVGQSKDENIHTSHITQDEFQRNSDRNMEEHEEMGNDCVSKKQMP
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KSEESPVYSNSSVRNELPMHHNSSRKSTKKTNQSSKNIRKKTIPLKRQKTATK
GNQRVQKFLNAEGSGGIVGHDEISRC SLSEPLESDEADLAKKKNLDCSRSTRS
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YLMSGKNDVDDEEVHGSSDDSKQSKVIPKNRIHHKLVLPSNTPNVRRTKRTR
LKPLEYWRGERIDYQGRPSGGFVISGVLSPDTISSKRKAKENIGKVNKKSNNK
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VKHGELKVYKTLDTPTFFSTGKLILGPQEEKGKQHVGDILVFYVNF GDLLCTL
HETPYILSTGDSFYVPSGNYNKNLRNEESVLLFTQIKR

FIGURE 13

DLG1



Chromosome position

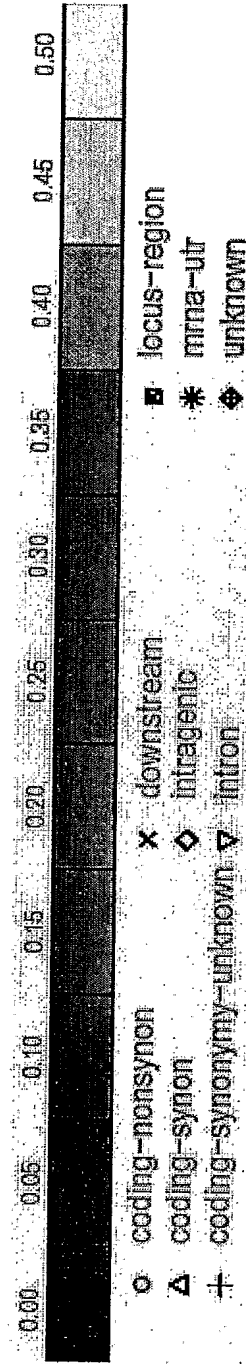
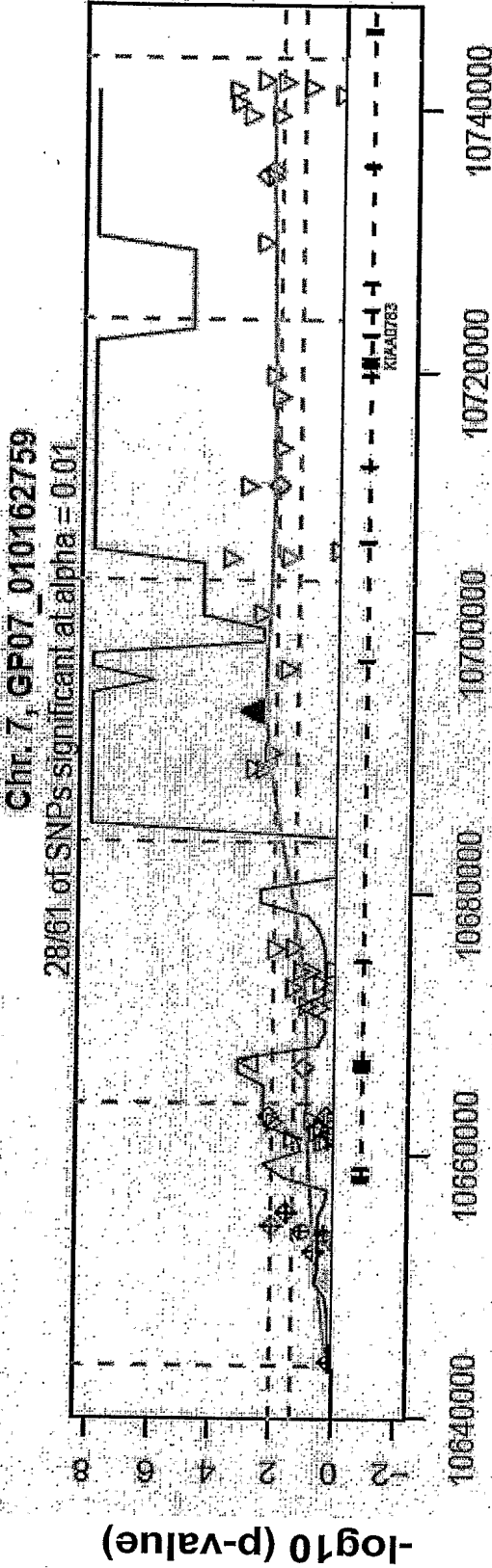


FIGURE 14

KIAA0783



Chromosome position

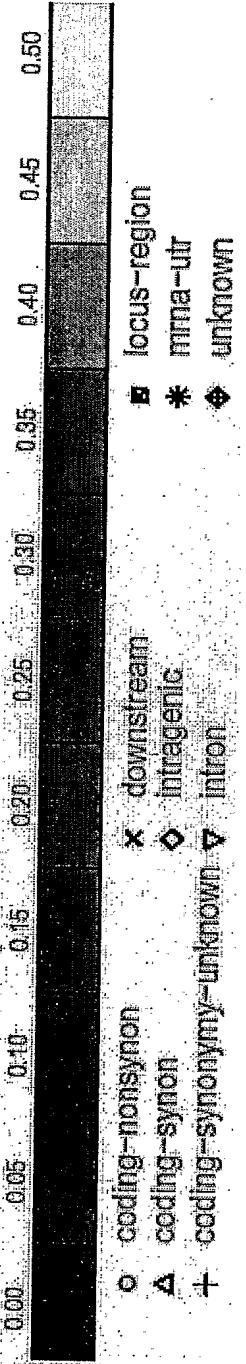


FIGURE 15

DPF3

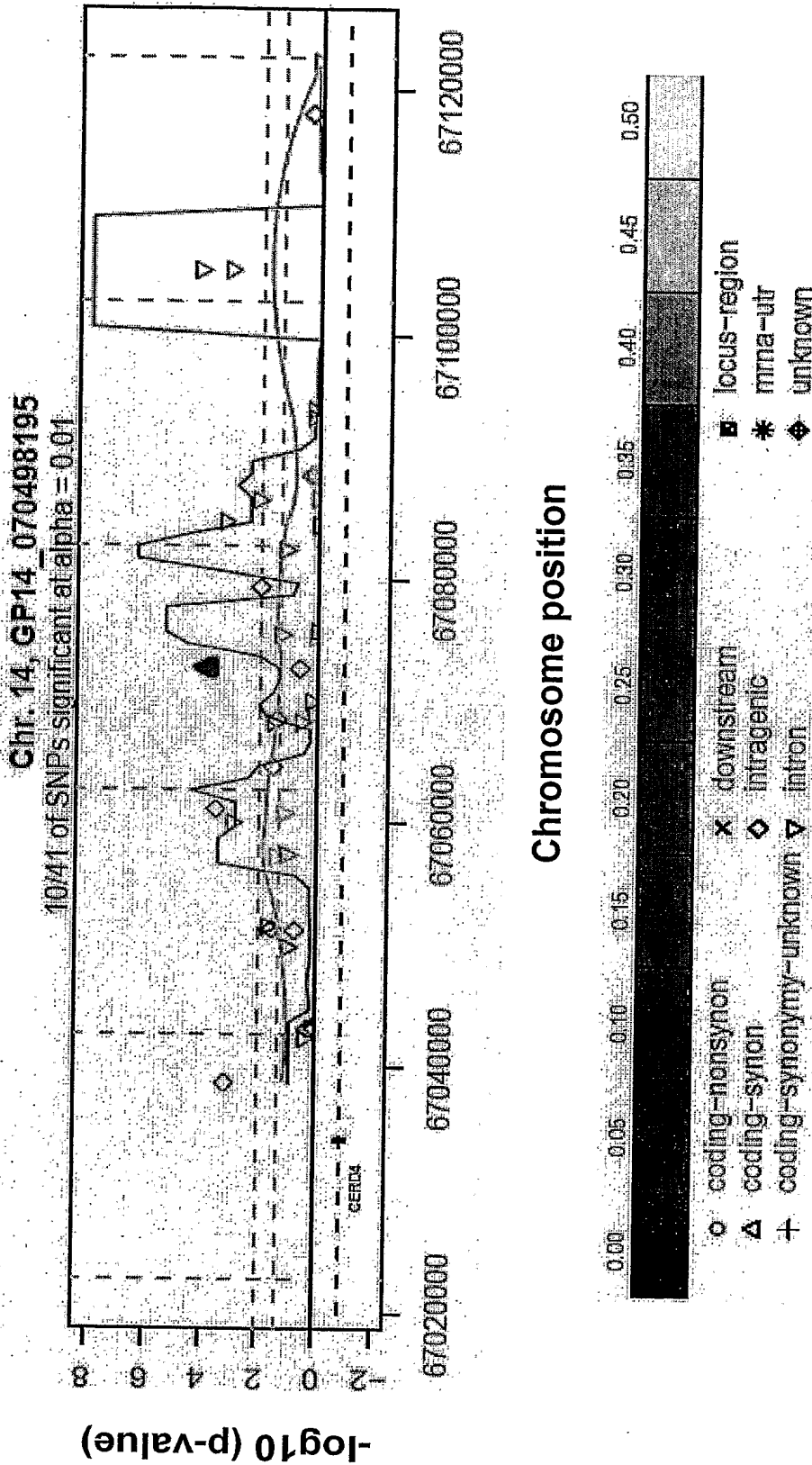
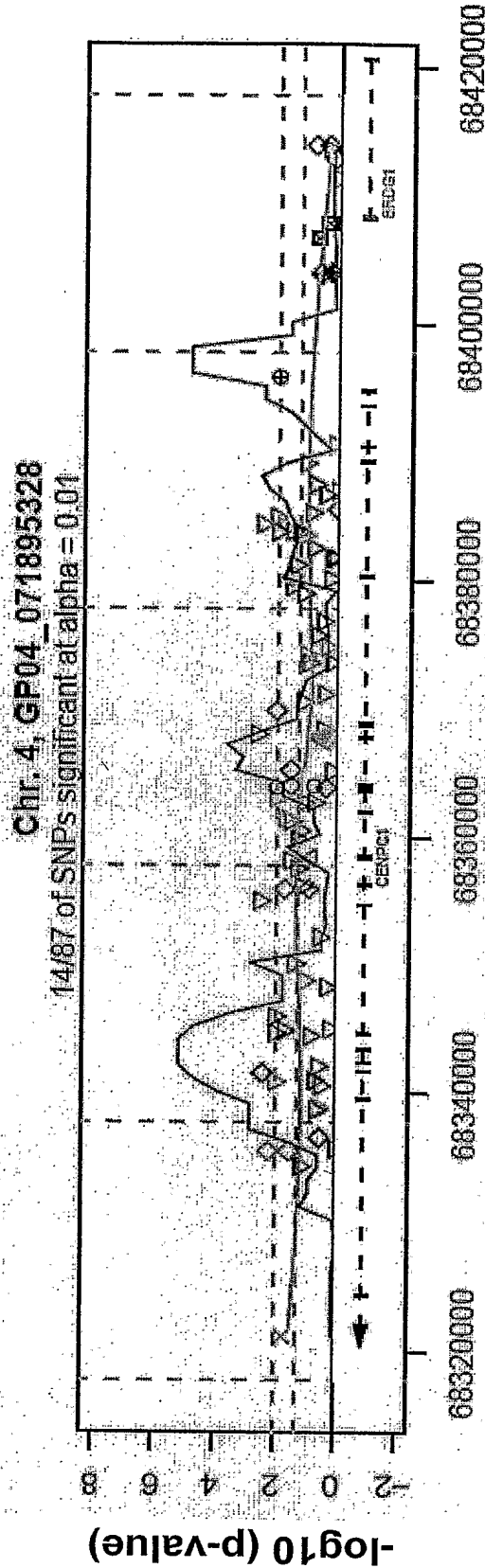


FIGURE 16

CENPC1



Chromosome position

